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SPLENECTOMY IN BLOOD DYSCRASIAS*

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BOSTON

THIS communication presents the results of splenectomy performed in patients with various blood dyscrasias who have been followed in the Blood Clinic of the New England Medical Center during the past ten years (July 1, 1939, through June 30, 1949). In the greater number of these patients, splenectomy was performed for congenital hemolytic anemia and primary thrombocytopenic purpura, and the results represent examples of the well established value of this operation. In some patients splenectomy was performed for other, less well defined conditions, and in others the indications for splenectomy might be called unusual or experimental. To determine the effect of splenectomy on blood dyscrasias the theoretical concept of hypersplenism and the influence of the spleen on the blood-forming organs and blood are major considerations. Both "primary" and idiopathic splenic disorders may occur, or the hypersplenism may be secondary to or symptomatic of other diseases. In the latter situation, the severity of the hypersplenic effects should influence the decision for splenectomy, rather than the question of whether or not splenectomy will cure the disease that the patient has. Thus, splenectomy may at times be of distinct value in a patient with an underlying disease that is itself not directly benefited by removal of the spleen.

Hypersplenism

Very little has been learned about the function of the spleen from animal experimentation. Most of our knowledge has come from clinical observation of patients with blood dyscrasias. The place of the spleen as a hemolytic organ is fairly widely recognized, but, in the absence of increased hemolysis, the effect of this organ on hematopoiesis is not so well known. One of us (W. D.) has maintained that in addition to its function in blood destruction, the spleen normally exerts an inhibitory effect on the bone marrow that may become increased when splenomegaly occurs.[1] Accentuation of this normal function is termed "hypersplenism" and manifests itself in increased hemolytic activity, in inhibition of hematopoiesis or by "blocking" the escape of mature cells from the bone marrow. In the two latter instances, various blood cytopenias result. These may take the form of a *total* reduction in all cellular elements in the blood (pancytopenia) or of *selective* cytopenias, with anemia, thrombocytopenia or neutropenia. In hypersplenism, the bone marrow is hyperplastic despite the presence of various types of cytopenia in the blood. Whether the concept of inhibition of the bone marrow by the spleen or that of splenic phagocytosis as espoused by Doan and his co-workers[2] is correct is not as yet definitely established.

In certain cases of both the acquired and congenital types of hemolytic anemia, the various effects of hypersplenism may be noted. Thus, in congenital spherocytosis, a depressive splenic effect upon the bone marrow may be observed, particularly in crisis.[3] During a major "crisis" splenectomy may be life saving.

Excessive blood destruction, together with inhibitory effects on the bone marrow, may result in various combinations of hemolytic anemia and the cytopenias. Individual patients may thus present varying hematologic patterns under substantially the same fundamental process.

That the spleen *normally* exerts some control over the bone marrow is not generally appreciated. This normal degree of inhibitory effect may become of some importance in certain bone-marrow diseases — for example, in hypoplastic anemia. Removal of the spleen in such cases may ameliorate the anemia. This effect of the spleen may be called "splenism," to differentiate it from hypersplenism.

From clinical observations it appears that certain forms of hypersplenism result from some primary or idiopathic disorder of the spleen, and others from a well defined coexisting disease. The best results of splenectomy are usually found in patients with primary splenic disorders. This is well exemplified by the results of operation in

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"primary" or idiopathic thrombocytopenic purpura, splenic neutropenia and splenic pancytopenia. On the other hand, the beneficial effects of splenectomy in patients with hypersplenism secondary to known disease may also be striking. It is in this group that difficult decisions for or against splenectomy arise. Some of the numerous causes of splenomegaly, usually with cytopenias, are as follows: certain infectious states (nonpyogenic), including rheumatoid arthritis and Boeck's sarcoid, hypertension of the portal and splenic veins (congestive splenomegaly), excessive cellular proliferation (in certain cases), excessive red-cell destruction (hemolytic anemias), disorders of lipid cellular metabolism, primary tumors and cysts of the spleen and idiopathic types (physiologic hyperactivity). Hypersplenism not infrequently develops in patients with splenomegaly caused by one of these states, and although many of them are not benefited by splenectomy, an indication for the operation may arise at some time during the course of these diseases.

Results of Splenectomy and Indications for Operation

Table 1 presents the results of splenectomy in 220 patients according to a classification based on the physiologic concept of hypersplenism, rather than on the more familiar one that considers each disease as a separate entity. It is possible in this manner to discuss the indications for splenectomy under three main headings: the hypersplenic hemolytic anemias, the hypersplenic cytopenias and "splenism," or the normal but adverse inhibitory influence of the spleen. Combinations of hemolytic and inhibitory splenic overfunction exist, but usually one or the other predominates.

Table 1. *Results of Splenectomy in 220 Cases of Blood Dyscrasias.*

Classification	No. of Cases	Good Results %
Hemolytic anemias:		
Congenital spherocytic anemia	38	100
Acquired hemolytic anemia:		
Primary	34	50
Secondary	18	33
Hypersplenism with cytopenias:		
Thrombocytopenic purpura (idiopathic)	92	61-80
Splenic pancytopenia and neutropenia:		
Primary	20	81
Secondary	14	71
"Splenism":		
Hypoplastic anemia	4	50

Whenever splenectomy is considered for patients with blood dyscrasias, the bone marrow should be shown either by aspiration or trephine biopsy to exhibit a degree of hematopoiesis that is at least normal. The prime exception to this is in the hypoplastic anemias, which are usually congenital. Here, although the bone marrow is hypocellular, a fair number of megakaryocytes should be found before one can consider that splenectomy is warranted. In most cases in which splenectomy is indicated, the bone marrow is actually hyperplastic, and, indeed, it is seldom possible to expect good results from splenectomy otherwise. For example, the bone marrow in primary thrombocytopenic purpura should contain an abundance of megakaryocytes, and in splenic neutropenia, granulopoiesis should be active. There are, of course, exceptions to this rule in unusual cases, as pointed out below.

The following discussion emphasizes the more unusual indications for splenectomy, with less attention to the well established indications.

Hemolytic Anemias

Congenital Spherocytosis

The diagnosis and indications for splenectomy in congenital spherocytosis are well known and require little discussion. Except for the failure to remove accessory spleens at the time of operation, uniformly good results should be obtained in all cases.[4] Cholecystectomy for coexisting gallstones is frequently necessary, and in most cases may be done at the time of splenectomy. The important aspect of the surgery of congenital spherocytosis is the question of operation during hemolytic crisis. It is our belief that splenectomy should be done during crisis if the fulminating process does not seem alleviated by a few blood transfusions. We find that "emergency" splenectomy, as advocated by Doan and his group, is rarely necessary; that it is better to prepare the patient by transfusions, fluids and other means before operation is performed. There were 38 patients with congenital spherocytosis in this group, all of whom obtained a complete remission.

Acquired Hemolytic Anemias

Splenectomy was performed in 52 cases in this series for acquired hemolytic anemia. The decision for operation in this group can be made only after careful study and after medical measures have failed.

Primary. Thirty-four of the 52 cases were considered to be of the primary or idiopathic type. Half these patients (50 per cent) obtained a complete remission after splenectomy. Not all the patients in this group were studied by such recently developed procedures as the Coombs antiglobulin test and bovine albumin titration, which are important diagnostic tools. Useful criteria in establishing this diagnosis include reticulocytosis, spherocytosis, normoblastic hyperplasia in the bone marrow, increase in the serum bilirubin, increase in output of fecal urobilinogen, circulating antibodies at 37°C. in saline solution or albumin or both, positive Coombs test and markedly diminished survival time of transfused normal red cells.

Secondary or symptomatic. In the acquired hemolytic anemia secondary to other diseases, many of the factors essential for the diagnosis of the primary type may not be fulfilled, but the increased hemolytic activity of the spleen may, in certain cases, be relieved by splenectomy. Splenectomy was performed in 18 cases in this group; only a third were benefited by operation. Table 2 lists the diseases that were the apparent cause of this secondary hypersplenism with hemolysis. The results in patients with leukemia and Hodgkin's disease have not been sufficiently good to warrant recommending splenectomy. The patients who were operated upon showed a severe hemolytic process that in itself seemed sufficient to justify the use of splenectomy at least experimentally. Examples of good results in secondary acquired hemolytic anemia were provided by 2 cases (Fig. 1 and 2).

TABLE 2. *Etiologic Diseases in 18 Cases of Acquired Hemolytic Anemia (Secondary or Symptomatic Type).*

DISEASE	NO. OF CASES
Dermoid cyst of ovary	1
Cirrhosis of liver	1
Chronic lymphocytic leukemia	4
Hodgkin's disease	2
Reticulum-cell sarcoma	2
Periarteritis nodosa	2
Sickle-cell anemia (with crises)	2
Mediterranean anemia	4

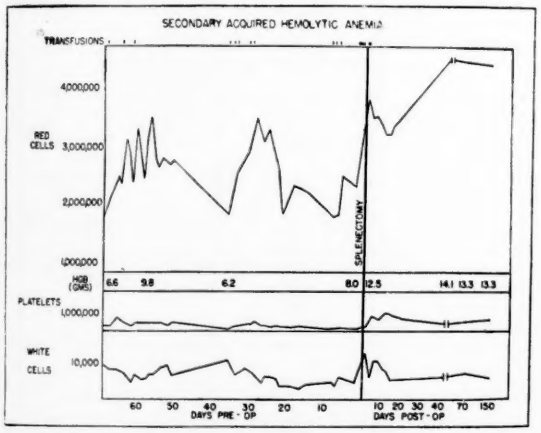

FIGURE 1. *Acquired Hemolytic Anemia with Reticulum Cell Sarcoma of the Ileum in L. P. (Case 1).*

The patient, a thirty-five-year-old man, was well until eight months before admission to the New England Center Hospital on April 28, 1949. Chief complaints were weakness and pallor. A diagnosis of acquired hemolytic anemia was made on the basis of splenomegaly and the hematologic findings: spherocytosis, reticulocytosis, bilirubinemia, presence of circulating antibodies, positive Coombs test, increased fecal urobilinogen excretion. Normoblastic hyperplasia of the bone marrow was found. He was given several transfusions without improvement. Splenectomy was performed on July 7, when a tumor of the lower ileum was discovered and a right hemicolectomy carried out. The patient's general condition and blood picture rapidly improved. Histologic diagnosis of the tumor proved it to be reticulum-cell sarcoma of the ileum, with metastasis to the regional lymph nodes. (The rise in red-cell count just prior to splenectomy was due to preoperative transfusions.)

Although the results of splenectomy for the entire group are by no means brilliant, the occasionally good results in individual patients who were desperately ill warrant consideration of the operation in similar cases.

HYPERSPLENISM WITH CYTOPENIAS

Selective effects on the cellular elements of the blood may occur as a result of hypersplenism.[2] Although idiopathic thrombocytopenic purpura has been treated by splenectomy for many years it is only recently that splenic neutropenia and splenic pancytopenia have been recognized and successfully treated by splenectomy. We have divided the cytopenias into the primary or secondary types depending upon whether or not there appeared to be an underlying causative disease.

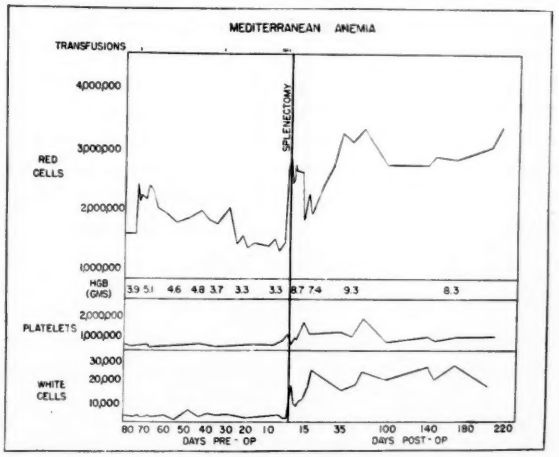

FIGURE 2. *Mediterranean Anemia with Severe Hemolytic Anemia in J. C. (Case 2).*

This patient, a twenty-nine-year-old man, was treated for ten years by medical measures, including blood transfusions at intervals. Recently, the anemia had become worse and on admission the red-cell count was 1,260,000, with 3.3 gm. of hemoglobin, bilirubinemia and a markedly increased fecal urobilinogen output. Transfusions of large quantities of blood seemed to help the hemoglobin level very little. There was an associated pancytopenia and reticulocytosis. The bone marrow was very hypercellular. On January 13, 1949, a very large spleen was removed. Subsequent to splenectomy the red-cell count and hemoglobin steadily rose, and although the patient is still anemic he is able to carry on all normal activities and is in better physical condition than he has been in the past five years. The figure graphically illustrates the effect of splenectomy. (The rise in red-cell count just prior to splenectomy was due to the transfusions.)

Idiopathic Thrombocytopenia Purpura (Primary)

The primary or idiopathic type of thrombocytopenic purpura usually responds to splenectomy; purpura of chemical, allergic or leukemic origin is not benefited and may even be made worse. All care must be taken to establish a correct diagnosis. The idiopathic type, in which the primary disorder often seems to rest in the spleen, has the characteristic bone-marrow findings of an abundance of megakaryocytes, which in addition to the other well known diagnostic criteria is essential for the diagnosis. The megakaryocytes are seemingly unable to form platelets but usually recover this func-

tional capacity upon removal of the spleen. In this series of 92 patients with idiopathic or "primary" thrombocytopenic purpura, 61 per cent achieved a complete and sustained remission after splenectomy.

In an additional 19 per cent some benefit was obtained by splenectomy, since there was a definite symptomatic relief with improvement in the hemorrhage state although the hematologic response was not complete. In these patients, either thrombocytopenia has persisted in the absence of symptoms or mild recurrences of purpura have appeared since operation. Of the various blood dyscrasias, idiopathic thrombocytopenic purpura is among those most successfully treated by splenectomy, and in this series splenectomy was performed more commonly for this disease than for any other. Recurrence of the disease may at times follow failure to find or to remove accessory splenic tissue. In children it is wise to delay decision for splenectomy, since spontaneous remissions are frequent. However, in adults with active bleeding from mucous membranes, delay may be fatal because of the danger of cerebral hemorrhage.

Splenic Pancytopenia and Neutropenia

Reduction in all cellular elements of the blood from hypersplenism or pancytopenia is much more frequent than neutropenia alone. Twenty-six of the patients in this series were subjected to splenectomy for splenic pancytopenia, and 8 for splenic neutropenia. In approximately half the patients with pancytopenia there was an associated hemolytic anemia as well. As we have previously stated, combinations of the hemolytic and cytopenic types of hypersplenism may coexist. Some degree of thrombocytopenia is also commonly found in cases of splenic neutropenia.

TABLE 3. *Etiologic Diseases in 14 Cases of Hypersplenism with Cytopenias (Secondary or Symptomatic Type).*

DISEASE	NO. OF CASES
Rheumatoid arthritis	2
Syphilis	2
Cirrhosis of liver	4
Gaucher's disease	1
Boeck's sarcoid	1
Malarial splenomegaly	1
Hodgkin's splenomegaly	1
Leukemic splenomegaly	2

When the cytopenias are primary or seem to be of splenic origin alone, the results of operation are better than when the cause is a hypersplenism secondary to other diseases. Twenty cases in this series were of the primary type of hypersplenism with pancytopenia and neutropenia. Eighty-one per cent (18 patients) had a remission subsequent to splenectomy. In 14 cases pancytopenia or neutropenia was secondary to known diseases (Table 3). Seventy-one per cent of these patients obtained a hematologic remission of their cytopenia after splenectomy although the underlying disorder remained unchanged. It should be stressed that the bone marrow in cases of supposed hypersplenism with cytopenias must be normal or hyperplastic if a good result is to be expected of splenectomy. Care must be taken to rule out such diseases as aleukemic leukemia, myelosclerosis with myeloid metaplasia of the spleen and lymphoma of the spleen. Two cases showing a satisfactory remission of splenic pancytopenia after splenectomy are illustrated (Fig. 3 and 4).

SPLENISM

We propose the term "splenism" for the state in which the normal inhibitory action of the spleen on the bone marrow is conceivably deleterious.

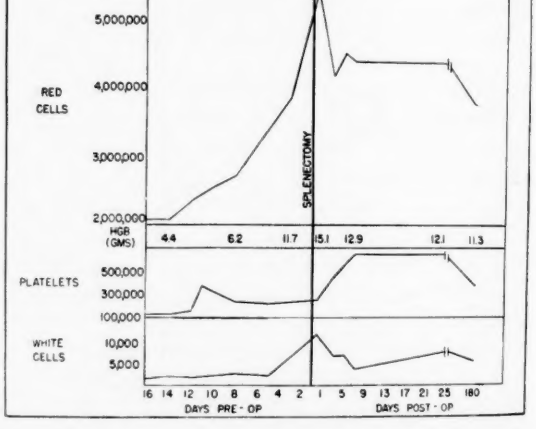

FIGURE 3. *Pancytopenia with Primary Hypersplenism in M. K. (Case 3).*

This patient, a twenty-seven-year-old woman, on admission to the New England Center Hospital on June 6, 1949, complained of weakness, pallor, cervical adenitis and fever of two weeks' duration. She had previously been treated for a year symptomatically for anemia. A palpable spleen was found, and the hematologic findings showed a decrease in the cellular elements of the blood. The bone marrow proved to be hypercellular, with adequate megakaryocytes and granulocytic hyperplasia. Erythropoiesis was normal. After splenectomy there was a prompt restoration of the blood picture toward normal values. (The marked rise in red-cell counts prior to operation was due to the use of transfusions.)

Splenectomy was advised and carried out in 4 patients with the congenital and familial types of hypoplastic anemia, including the Fanconi syndrome.

The results of splenectomy in this group are not conclusive because of the small number of patients involved; furthermore, the indications for splenectomy cannot be said to have been definitely established here. However, in 2 of the 4 patients with congenital hypoplastic anemia, substantial improvement in the blood picture and in general health followed splenectomy. The spleen is not enlarged in these patients, and we have postulated that splenectomy removes the normal degree of

inhibition exerted upon the bone marrow. Splenectomy is performed in the absence of a hyperplastic bone marrow, and in this regard an exception is taken to the general rule stated above.[5] Figure 5 shows the results of splenectomy in a patient with this disease.

Technic of Splenectomy

The operation of splenectomy has been fully described in the recent literature.[6, 7] In the usual case, in which the spleen is not adherent to the diaphragm and not unusually large, it may be freely mobilized — first by incision of its avascular attachments to the kidney and diaphragm, followed by severance of the gastrosplenic ligament and a small portion of the gastrocolic ligament. Then the tail of the pancreas may be detached from the hilus and ligation of the splenic artery and vein follows in that sequence. The operation is easily performed in most cases, but since it is done only occasionally in many hospitals, there is some value in discussing the important aspects of the procedure.

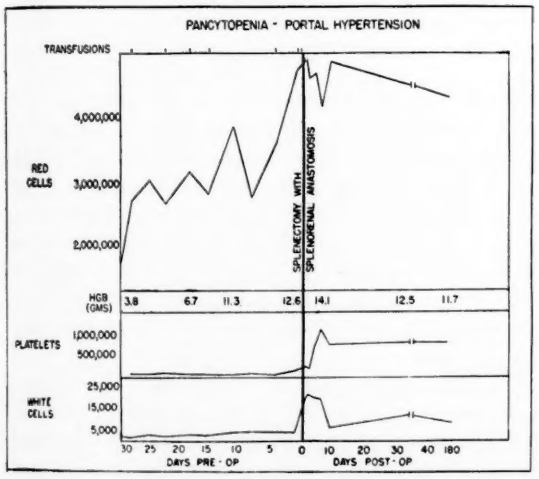

Figure 4. *Pancytopenia with Hypersplenism Secondary to Cirrhosis of the Liver and Portal Hypertension (Case 4).*

This patient, a ten-year-old girl, was admitted on April 22, 1949, to the Boston Floating Hospital with a history of acute hepatitis three years previously, since which she had been fairly well until three months before admission. At that time fever, cervical adenitis, sore throat and weakness developed. Splenomegaly was found, with definite evidence of reduced liver function. Anemia, leukopenia and thrombocytopenia were evident in the peripheral blood, with a hyperplastic bone marrow containing increased megakaryocytes. At operation the portal venous pressure was found to be elevated (equivalent to 300 mm. of water). A splenorenal venous anastomosis was performed in addition to splenectomy. (The rise in red-cell count prior to splenectomy was due to the use of transfusions.)

There are three important points in the technic of splenectomy that are worthy of comment. The first consideration to be borne in mind is that a careful detachment of the stomach from the spleen will avoid injury to this organ, which is in close proximity to the spleen, particularly superiorly. Secondly, Singleton[8] has stressed the value of a preliminary ligation of the splenic artery near its origin as a wise and useful step in difficult cases. This maneuver is particularly useful when a large spleen adherent to the diaphragm must be removed. The third contribution comes in the use of the combined abdominal and thoracic exposure as recommended by Carter.[9] The extension of any sort of left-sided abdominal incision through the ninth or tenth intercostal space offers an excellent approach for the removal of large spleens that have become firmly attached to the diaphragm and parietes. Better yet, resection of the ninth or tenth rib may be done. The number of cases in which additional thoracic exposure is needed is small. Perhaps the large spleen seen in portal hypertension

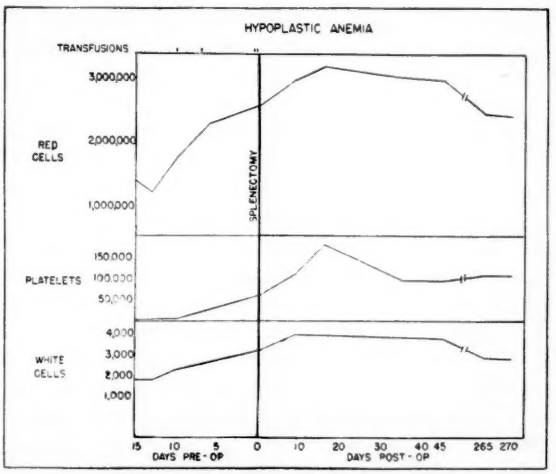

Figure 5. *Familial Hypoplastic Anemia of Childhood in R. G. (Case 5).*

This patient, a ten-year-old boy, was admitted to the Boston Floating Hospital in October, 1944, with a history of epistaxis and bleeding from the gums. He was one of 14 siblings, 5 of whom had exhibited a similar disorder, resulting in death. Examination of the peripheral blood showed a pancytopenia without bilirubinemia. There was no evidence of splenomegaly. Bone-marrow studies by both puncture and trephine methods showed a hypocellular marrow exhibiting normal development of granulocytes and smaller numbers of megakaryocytes. Splenectomy was performed on November 1, and a relatively normal spleen removed. Marked symptomatic improvement followed, with improvement in the blood picture. The patient has remained symptomatically and hematologically improved since operation, although the blood picture has by no means reached normal values. (The rise in red-cell count before operation was due to the use of transfusions.)

associated with cirrhosis of the liver and requiring splenorenal venous anastomosis represents the principal indication for the extension of the abdominal incision into the chest. This combined abdominothoracic exposure is not to be confused with the transthoracic approach, in which entrance into the abdomen is obtained via the diaphragm only.

A caution is necessary regarding the use of the transthoracic route in which splenectomy is accomplished through the diaphragm after posterolateral thoracotomy. Some surgeons have advocated the use of this approach for splenectomy,

even in cases in which the operation is relatively easily performed by abdominal incision. The fact that a freely movable spleen may be easily removed transthoracically does not necessarily imply that this route is the preferred one. We do not believe that it is a good choice of approach for splenectomy. Careful exploration of the abdomen is a necessary part of a celiotomy for splenectomy in the blood dyscrasias not only for the detection of accessory spleens but also for the discovery of associated lesions or diseases that might have some etiologic relation to the existing hypersplenism. This cannot be accomplished adequately through the thorax and diaphragm. Blockage either in the liver or in the tributaries of the portal vein cannot be adequately explored transthoracically. Intestinal and ovarian tumors associated with acquired hemolytic anemia may be missed if exposure of the abdominal cavity is inadequate. In addition, cholecystectomy may usually be performed at the same time as splenectomy in cases in which congenital spherocytosis and gallstones are associated, provided celiotomy is performed. Another disadvantage of the transthoracic route is met in the difficult splenectomy with perisplenitis and vascular diaphragmatic attachment. Here, upon incision of the diaphragm, excessive bleeding may be encountered before the splenic artery can be ligated. A combined abdominothoracic incision is the operation of choice if the additional exposure is necessary, since it allows preliminary abdominal exploration and ligation of the splenic artery.

The mortality after splenectomy will not be great if patients are carefully selected and prepared by close co-operation of the surgeon and internist. The use of fresh blood is desirable, and in some cases washed red-cell transfusions are needed.[10] A trained team of hematologists is essential for this work. Preoperative transfusions are very valuable, but if rapid disappearance of transfused blood ensues in the hemolytic anemias, splenectomy should be done without delay. During the postoperative period, the blood picture must be observed at least daily since transfusions may be needed. Postsplenectomy venous thrombosis is exceedingly uncommon despite the appearance of great numbers of platelets, which is noted frequently, and in our experience the use of anticoagulants has rarely been necessary.

During the ten-year period of this study splenectomy has been performed in our clinic by several surgeons, with a relatively low mortality. The risk of operation is not sufficiently great to contraindicate surgery in patients who have a good chance of benefit by removal of the spleen.

We have managed 49 of these patients together on a combined spleen service in the last three years. Two patients had splenorenal anastomoses in addition to splenectomy. There were 3 hospital deaths after splenectomy among these 49 patients. The first occurred in a patient with thrombocytopenic purpura in her fourth episode of severe hemorrhage. Continued bleeding from the operative site, in addition to increased subcutaneous bleeding, was the cause of death. In this case splenectomy may have been a precipitating factor in the patient's death. Bleeding after splenectomy in cases of idiopathic thrombocytopenic purpura is uncommon, and we believe from experience in this case and in others that have not proved fatal that patients in their third or fourth episode should perhaps not be operated on at the time of acute purpura but should be tided over the critical period. The two other deaths occurred in patients with acquired hemolytic anemia whose response to splenectomy was poor. Both had severe hemolytic anemia, one secondary to known leukemia; the other was of idiopathic origin despite careful study. The operation of splenectomy alone did not appear to have an adverse effect, since the patients seemed to improve for a short period postoperatively.

Summary

The results of splenectomy in 220 patients with blood dyscrasias are presented, and the indications for splenectomy in relation to the concept of hypersplenism and to the normal function of the spleen discussed. The indications for splenectomy in blood dyscrasias in which the decision for operation is more difficult than in such well established diseases as congenital spherocytic anemia and idiopathic thrombocytopenic purpura are commented upon.

Acquired hemolytic anemia and hypersplenic cytopenias secondary to existing diseases may be ameliorated by splenectomy in a substantial number of patients who would otherwise have a poor prognosis. Careful selection of patients by the internist, with adequate preoperative preparation, is essential for the best results.

References

1. Dameshek, W., and Estren, S. *The Spleen and Hypersplenism.* New York: Grune & Stratton, 1947.
2. Wiseman, B. K., and Doan, C. A. Newly recognized granulopenic syndrome caused by excessive splenic leukolysis and successfully treated by splenectomy. *J. Clin. Investigation* **18**:473, 1939.
3. Dameshek, W., and Bloom, M. L. Events in hemolytic crisis of hereditary spherocytosis, with particular reference to reticulocytopenia, pancytopenia and abnormal splenic mechanism. *Blood* **3**:1381-1410, 1948.
4. Curtis, G. M., and Movitz, D. Surgical significance of accessory spleen. *Ann. Surg.* **123**:276-298, 1946.
5. Estren, S., and Dameshek, W. Familial hypoplastic anemia of childhood: report of eight cases in two families with beneficial effect of splenectomy in one case. *Am. J. Dis. Child.* **73**:671-687, 1947.
6. Lahey, F. H., and Norcross, J. W. Splenectomy: when is it indicated? *Ann. Surg.* **128**:363-378, 1948.
7. Cole, W. H., Walter, L., and Limarzi, L. R. Indications and results of splenectomy. *Ann. Surg.* **129**:702-723, 1949.
8. Singleton, A. O. Splenectomy. *Ann. Surg.* **115**:816-820, 1942.
9. Carter, B. N. Combined thoracicoabdominal approach with particular reference to its employment in splenectomy. *Surg., Gynec. & Obst.* **84**:1019-1028, 1947.
10. Dameshek, W., and Neber, J. Transfusion reactions to plasma constituent of whole blood: their pathogenesis and treatment by washed red-blood cell transfusions. *Blood* **5**:129-147, 1950.

ACUTE GENERAL EDEMA OF THE BRAIN IN CHILDREN WITH HEAD INJURIES*

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A FEW months ago I presented to the New England Surgical Society some observations[1] based on a series of 7 children, varying in age from ten months to eleven years, who had presented symptoms and signs strongly suggestive of extradural hemorrhage, but whose recovery without operation was so rapid and complete as to cast doubt on this diagnosis. In most cases the child fell and struck his head on the floor or ground, and in about half, there was initial unconsciousness with fairly prompt recovery from this state. Only 2 of the children suffered from traumatic shock. At an interval varying from fifteen minutes to six hours, focal signs developed. These included one-sided reflex changes indicating cortical involvement; Jacksonian convulsive movements, or a combination of Jacksonian and generalized convulsions; and one-sided paralyses of differing degrees. Since it is my practice not to do lumbar punctures in the presence of shock, or when acute intracranial bleeding is suspected, evidence that might have been gained from the cerebrospinal fluid during the acute phase was not available, but punctures done soon after the subsidence of acute symptoms showed essentially normal findings. About half the patients had associated skull fractures. Clinical evidence of this condition disappeared completely in from three to twenty-four hours. The course of events in these cases presented considerable difficulty in diagnosis. It was evident that there had not been time for the absorption of an extradural hematoma or of a subdural collection of blood causing the same sort of local pressure; the possibility that a previously localized blood mass in either the extradural or subdural space had spread into a thin, nonirritating layer seemed unlikely in the absence of residual effect; local contusion of the cortex, with actual tissue damage, could explain the motor and reflex involvement, but recovery occurred too soon; therefore, I came to believe that an acute focal edema of the brain was the most reasonable explanation. An eighth case was reported, in which a four-year-old girl was knocked down and became unconscious at once. She regained consciousness in a few minutes and vomited, but lapsed into unconsciousness again in fifteen minutes. She then had convulsive movements of both arms and legs, the left side being definitely more involved than the right, became completely comatose and finally stopped breathing. Under artificial respiration and oxygen, a right subtemporal exploration was made, but no extradural or subdural bleeding or clot was found; the underlying brain was swollen and edematous and had no pulsations, and after exploration of an area about 10 cm. in diameter the swelling and edema subsided, normal brain pulsations returned, and natural breathing was resumed. Within a few hours the girl was fully conscious, oriented, co-operative and apparently well, and I believed that this operation confirmed my impression that this clinical picture was due to an acute focal edema. Consultation of the writings of others interested in this general subject showed that these observations were not original and that Walton,[2] and Walton and Brooks[3] had reported such conditions fifty years ago and had arrived at the same conclusion. In recent publications, however, little or no attention has been paid to this syndrome of symptoms and signs simulating middle meningeal hemorrhage. The present communication is a continuation of the observations begun in my previous paper.

I have had 1 other case of acute focal edema shown at operation. On January 4, 1949, a three-year-old girl, recently exposed to whooping cough, was struck on the right forehead by a headlight of an automobile. Her father picked her up and carried her into the house, where she whimpered a little, said a few words without thoroughly regaining consciousness and vomited several times. She was taken to the Rhode Island Hospital about half an hour after the accident. She was then in moderate traumatic shock, with ashen-gray color, depressed rectal temperature, elevated pulse rate and shallow respiration, but normal blood pressure. She was semicomatose, with very little response to any stimulus. There was a hematoma of the scalp in the right frontal region, but there was no bleeding from any cranial orifice. The eyes were conjugately deviated to the right and showed some lateral nystagmus, with the long component to the right; the pupils were equal and reacted only slightly to light, but demonstrated rapid spontaneous dilatations and contractions. At first, the left arm and leg moved slightly in response to painful stimuli, but there was no corresponding movement of the right arm and leg; later Jacksonian convulsive movements of the right side of the face and the right arm and leg developed. She had no deep tendon reflexes, but had bilateral dorsiflexion of the great toe on plantar stimulation. The physical examination was otherwise negative, except for coarse rhonchi in both lungs and an abrasion of the left leg. She was given shock treatment, and it was believed that she might have acute focal edema,

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extradural or subdural bleeding, or a localized brain contusion. When the focal signs persisted, however, and the coma deepened it was decided that intracranial bleeding must be ruled out, and a left subtemporal exploration was made. There was no evidence of contusion of the soft tissues or of fracture in the area exposed. When the bone was opened no extradural bleeding or clot was found, and the dura was tense but not discolored. On deeper exploration no subdural bleeding or clot was evident, but the brain was swollen and edematous and did not pulsate. The usual 10-cm. area was investigated, but no blood or hygroma was found. At the end of this procedure the brain was much less edematous, it no longer tended to herniate into the bone opening, and it had normal pulsations. Since the child was completely comatose at the beginning of the operation, no anesthesia was used; during the closure of the wound, however, she began to show some response to pain, the breathing became less shallow, and she began to move the right arm and leg. Within a few hours she was conscious and co-operative, and was apparently normal from a neurologic standpoint.

Examinations made after the operation showed a white-cell count of 27,700, which fell in a day or two to 10,000; and x-ray films disclosed a linear fracture of the left temporo-occipital region without depression, no injury of the cervical spine, and appearances in the chest consistent with bronchopneumonia. This lung condition responded well to treatment with penicillin, but because of her exposure to whooping cough the child was transferred to the Chapin Hospital, where she continued to make a good recovery. She was discharged well at the end of three weeks, and has remained well until the present time. Here, again, I believe that the actual demonstration of swelling and edema of the motor cortex in the absence of bleeding or intracranial hematoma shows that acute focal edema can cause the condition described.

The first child on whom I operated had evidence of an acute process involving the motor cortex, chiefly on the right side, but also to a lesser extent on the left, with subsequent spread to the medullary centers and resulting failure of respiration; the second had a similar process affecting most definitely the motor cortex on the left side, but with beginning spread to the medulla. In both cases there was visible swelling and edema of the temporal cortex, and rapid clearing of symptoms and signs followed mechanical decompression. In a certain number of children, however, I have met with a condition analogous to this, but without focal signs, and it is this condition that I should now like to discuss.

The typical history of a child with this syndrome corresponds in general to the following description. He falls, striking his head either on the front or on the back quite violently, but does not lose consciousness. About half an hour later he becomes unconscious and rapidly lapses into coma, from which he cannot be aroused, so that he is brought to the hospital. On arrival at the accident room his color is poor, his breathing is stertorous and labored and may even have Cheyne–Stokes characteristics, his pulse may be full and bounding or weak and rapid, and he appears to be in imminent danger of death from medullary compression. He is looked upon as being dangerously ill, and is admitted to the hospital as having unlocalized intracranial hemorrhage. He usually has no reflex responses and little or no spontaneous movement of the extremities. There is no evidence of traumatic shock, and the blood pressure is not depressed. Preparations are made for an emergency exploration, but before they can be completed the patient begins to show improvement. This improvement, once begun, progresses quickly, and the child is usually apparently well within two hours of the onset of the condition.

In the course of caring for over 500 children with head injuries at the Rhode Island Hospital during the past six years, I have treated 8 children presenting this general picture. As with acute focal edema, I have not met with this condition in an adult, although far more adults than children are seen at the hospital. The patients have varied in age from one year to twelve; 5 have been boys, and 3 girls. In most cases the child has fallen from heights varying from 3 to 30 feet and has then banged his head; 2 children have been thrown for some distance by an automobile and have then struck their heads. Linear fracture of the vault without depression has been found in 3 cases; in no patient has there been fracture of the base. There was initial unconsciousness followed by a lucid interval in only 1 case; this patient was also the only one to have convulsions, which were generalized. About half the patients vomited before or after the acute episode. None of these patients had traumatic shock. The interval between the injury and the onset of symptoms varied from fifteen minutes to ten hours, the great majority having an interval of about half an hour. In most cases the condition cleared up within two hours of the onset; the longest period needed for clearing was six hours. For the reasons given above, the cerebrospinal-fluid findings during the acute phase are not known; spinal taps done soon after recovery from this stage have shown no abnormality except in 1 case, in which a protein value of 43 mg. per 100 cc. and 136 red blood cells per cubic millimeter indicated a probable associated mild contusion of the brain. The incidence of this condition, in my experience, is low, being somewhat under 1.5 per cent; the incidence of acute focal edema is a little over 1.5 per cent.

The first group of cases that I reported presented a clinical picture bearing a striking resemblance to that brought about by middle meningeal hemor-

rhage. I shall not review the reasons, already given, that led me to discard this as a diagnosis and convinced me that they had an acute focal edema, but I have twice, at operation, demonstrated cortical swelling and edema in an area where its presence could account for the clinical findings. The second group of patients, now under discussion, showed a condition of medullary compression consistent with severe bleeding within the head, without localizing signs. Here again, however, the rapid and complete clearing up of the evidences of involvement of the vital centers, without operative interference, and with no residual signs of permanent damage, almost certainly ruled out bleeding as the causal factor. None of these patients have been operated on, and no death resulted, so that actual demonstration of the pathologic processes involved has not been possible. In the light of previous experience, however, I am inclined to believe that these children had an acute general edema of the brain, analogous to and possibly related to the acute focal edema already shown to exist; in support of this belief, I shall briefly review some of the work that has been done in the study of compression of the brain.

According to Trotter,[4] "the surgery of head injuries as we receive it today comes down to us not only grounded in an immeasurably large experience, but encrusted with tradition embodying doctrines of which some are still useful and living while many have outlived their vitality and yet are unable to die." This observation, embodying the wisdom that can only come from thorough historical knowledge tempered by painstaking and understanding care of injured human beings, was made by one of the keenest recent students of head injuries, in an address on the evolution of the surgery of these conditions. To his doctrines, which are "still useful and living," should be added those which could still be useful but which have been buried alive in libraries, with an untouched card in a dusty catalogue as their only headstone.

The striking nature of head injuries has excited interest since the time when medical observations first began to be written down. The unknown author of the *Edwin Smith Surgical Papyrus*[5] made records of patients suffering from these conditions in this earliest known medical manuscript, and Hippocrates[6] and Celsus[7] wrote treatises about them. These early authors were concerned almost entirely with injuries to the skull, and regarded the fracture as the really important factor. One of the "encrustations" from which the subject still suffers is the prevalent notion that the presence or absence of fracture of the skull is of the greatest importance in determining the severity of a head injury, and I am sorry to have to say that the x-ray demonstration of such a fracture is, even today, widely used as the chief reason for admitting patients to hospitals. This primary interest in bone damage persisted until the late eighteen hundreds, but as early as the sixteenth century Ambroïse Paré[8] appreciated the role of extradural bleeding in compressing the brain and described the use of a leaden cannula "to give issue to the blood retained between the Skull and the Dura mater." At about this same time Paré[9] and Vesalius[10] each reported independently what has been generally accepted as the first proved case of brain compression from a subdural hemorrhage. In 1743, François Quesnay,[11] in one of the forgotten treatises embalmed in the literature, showed that the surgeons of Paris were well aware of brain compression from epidural spillage of blood, and that one of them, at least, knew something about subdural hemorrhage. In 1868, Jonathan Hutchinson[12] summed up the prevailing ideas on brain compression. He recognized four causes, — blood between the dura and bone, blood under the dura mater, pus between the dura mater and skull, and depressed bone fragments, — but he did not mention compression in the absence of some such foreign substance.

The widespread interest in things physiologic at the end of the nineteenth century brought about a better understanding of the cerebral circulation and an appreciation of the importance of compression of the brain without any of the causes mentioned by Hutchinson. In 1901 Cannon[13] made a careful study of the problem of intracranial pressure following trauma. He considered the following two theories then current:

> That sponsored by von Bergmann and by Hill, which held that, as a result of intracranial hemorrhage, blood stasis with tissue anemia was produced at the point of injury, and that there was a compensatory increase in the rate of blood flow in more distant areas with a consequent transudation of fluid that still further increased the cerebral anemia.
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> And that put forth by Courtney, who believed that there was a paralysis of the cerebral vasomotor centers with a consequent dilatation of blood vessels resulting in acute anemia of the brain substance, and that this brought about transudation of fluid, which could not be absorbed, with following increase of pressure.

Cannon believed that neither of these theories could be true, since both depended on mechanical filtration to produce a pressure greater than that of its source. He made interesting experiments and came to the conclusion that, at the moment of injury, the intracranial pressure rises to a height sufficient to check blood flow into the brain; that the primary loss of consciousness is due solely to this circulatory disturbance; that the brain tissue deprived of its blood supply undergoes chemical changes bringing about an increase in osmotic tension; and that this causes the passage of water into the tissue with the

creation of a vicious circle, and he believed that recovery, when it occurs, is due to diffusion of the products of destruction.

In 1908 Harvey Cushing[14] presented a thorough consideration of cerebral compression, including some of his own experimental work. He states the initial causes of local pressure as tumor, abscess, focal edema, vascular extravasation or an operative procedure, whereas meningitis, hydrocephalus, general edema, basal hemorrhage or sinus thrombosis may result in more widespread compression. This compression produces venous stasis, pressure on the capillaries and cerebral anemia, which, if it persists for any considerable time, is irreversible. In a local process, the effects of compression are confined to the region of the primary lesion for a time, but then spread to involve the entire brain and the vital medullary centers. And he also says, "We often see compression associated with an increase of fluid, as in the acute traumatic edemas — the so-called traumatic serous meningitis."[15] He describes the course of events in developing compression in terms of Kocher's four stages: a first stage of mild compression with compensation by rearrangement of the cranial content; a second stage of beginning failure of compensation by advancing anemia; a third stage of widespread capillary anemia with beginning medullary involvement and attempted compensation, as shown by a Cheyne–Stokes type of respiration; and a fourth stage of complete medullary failure, resulting in death. This concept of brain compression, based on clinical observation of a high order and on careful experimental studies, has not been disproved, and is probably as true and certainly as useful as when it was first put forth.

But, being human, physicians become tired of old concepts and search for something new, and are too prone to accept the new because it is different and up to date, without carefully assessing it in terms of the old. So it is now stated that there is no true edema of the brain, or that its role in the production of symptoms in brain conditions is unimportant. In 1939, Shapiro and Jackson[16] reported post-mortem studies showing that the swelling of the brain is due to ventricular distention and increased blood content, with no provable edema from a pathological standpoint. And there has been much discussion of the location of excess fluid, when it is found, and of the proper definition of edema. In careful and extensive pathological studies, however, Rand[17] and Rand and Courville[18] showed definite microscopical evidence of edema of brain tissue in patients and animals dying as the result of injury. Moritz[19] sums up these divergent views as follows: "Since there are as yet no generally accepted pathological criteria for the recognition of generalized cerebral edema, the problem must wait further investigation before it can be regarded as settled."

But the existence of clinical edema of the brain — that is, the visible presence of excess fluid outside cerebral vessels — is admitted by most men who have had wide experience in the treatment of patients suffering from head injuries. Thus, Munro[20] regards edema and congestion as most important factors in the production of symptoms, and Rowbotham[21] makes the following statements:

> That generalized edema can occur there is no doubt. When operating under local anaesthesia, I have occasionally found the brain, in the acute phases of a head injury, under such great tension that it bulged into the wound as soon as the dura was opened, and later at autopsy have been able to show that the increased tension was not due to hydrocephalus and could not have been due to the amount of blood extravasated. It cannot be objected that the increased tension found on surgical exploration was due to the anaesthetic because local anaesthesia does not affect the intracranial tension.

Summary

Observations on children with symptoms and signs strongly suggesting middle meningeal hemorrhage, but with such rapid disappearance of these indications as to cast doubt on the diagnosis, are presented. Consideration of the time elements present, the various pathologic processes that might be expected to bring about such a state, and the reports of others led to the conclusion that acute focal edema of the brain, with associated capillary anemia, best explained the condition. Two patients had visible clinical edema of the motor cortex, demonstrated at operation. In these cases there was a spread of the process bringing about involvement of the medullary centers such as is present in general brain compression. Observations on 8 other children, who, shortly after injury to the head, manifested alarming evidence of medullary compression without preceding focal signs, but who recovered rapidly and completely without operation, are also presented. In view of the actual demonstration of acute focal edema of the brain in 2 of the children in the first group, and in view of the striking similarity of the late stages of their condition to that of the children in the second group, it seems fair to assume that the presence of an acute general edema of the brain offers the most reasonable explanation for the interesting clinical picture now reported.

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References

1. Pickles, W. Acute focal edema of brain in children with head injuries. *New Eng. J. Med.* **240**:92-95, 1949.
2. Walton, G. L. Subarachnoid serous exudation productive of pressure symptoms after head injuries. *Am. J. M. Sc.* **116**:267-275, 1898.
3. Walton, G. L., and Brooks, W. A., Jr. Observations on brain surgery suggested by case of multiple cerebral hemorrhage. *Boston M. & S. J.* **136**:301-305, 1897.
4. Trotter, W. Address on evolution of surgery of head injuries. *Lancet* **1**:169-171, 1930.
5. Breasted, J. H. *The Edwin Smith Surgical Papyrus: Published in facsimile and hieroglyphic transliteration and commentary in two volumes.* Vol. 1. 596 pp. Chicago: University of Chicago Press, 1930. Pp. 158, 159 and 161.
6. Hippocrates. *On Wounds of the Head.* Translated by E. T. Withington. Vol. 3. 455 pp. London: William Heinemann, 1927. Pp. 7 ff.

7. Celsus. *De medicina.* Translated by W. G. Spencer. Vol. 3. 649 pp. London: William Heinemann, 1938. Pp. 475 ff.
8. Paré, A. *Oeuvres complètes.* Edited by J.-F. Malgaigne. Vol. 2. 811 pp. Paris: J.-B. Baillière. 1840. P. 63.
9. *Idem.* P. 25.
10. O'Malley, C. D., and Saunders, J. B. de C. "Relation" of Andreas Vesalius on death of Henry II of France. *J. His. Med. & Allied Sc.* 3:210-213, 1948.
11. Quesnay, F. Précis de diverses observations sur le trépan dans des cas douteux. *Mém. Acad. roy. de chir.* 1 (Part 1):311-382, 1743.
12. Hutchinson, J. Four lectures on compression of brain. *Clin. Lect. & Rep., London Hosp.* 4:10-55, 1867-68.
13. Cannon, W. B. Cerebral pressure following trauma. *Am. J. Physiol.* 6:91-121, 1901.
14. Cushing, H. Surgery of head. In *Surgery: Its principles and practice.* Edited by W. W. Keen. 5 vol. Philadelphia and London: W. B. Saunders Co., 1908. Vol. 3. Pp. 182 ff.
15. *Ibid.* P. 190.
16. Shapiro, P., and Jackson, H. Swelling of brain in cases of injury to head. *Arch. Surg.* 38:443-456, 1939.
17. Rand, C. W. Histologic studies of brain in cases of fatal injury to head. I. Preliminary report. *Arch. Surg.* 22:738-753, 1931.
18. Rand, C. W., and Courville, C. B. Histologic studies of brain in cases of fatal injury to head. II. Changes in choroid plexus and ependyma. *Arch. Surg.* 23:357-425, 1931. Histologic changes in brain in cases of fatal injury to head. III. Reaction of microglia and oligodendroglia. *Arch. Neurol. & Psychiat.* 27:605-644, 1932. Histologic studies of brain in cases of fatal injury to head. IV. Reaction of classic neuroglia. *Ibid.* 27:1342-1379, 1932. Histologic changes in brain in cases of fatal injury to head. V. Changes in nerve fibers. *Ibid.* 31:527-555, 1934.
19. Moritz, A. R. *The Pathology of Trauma.* 386 pp. Philadelphia: Lea & Febiger, 1942. P. 309.
20. Munro, D. *Cranio-Cerebral Injuries: Their diagnosis and treatment.* 412 pp. London: Oxford University Press, 1938. Pp. 117-121.
21. Rowbotham, G. F. *Acute Injuries of the Head: Their diagnosis, treatment, complications and sequels.* 288 pp. Baltimore: William Wood & Co., 1942. P. 55.

ABDOMINAL ANGINA

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IN MOST syndromes, so-called classic pictures develop as a result of the more severe manifestations of the disease. As knowledge increases, lesser forms are recognized. This is illustrated best in the literature of recent years by the more frequent recognition of milder, subacute and recurrent types of pancreatitis as against the more classic severe catastrophe. Similarly, in textbooks the subject of intra-abdominal vascular disease is usually confined to a discussion of massive mesenteric thrombosis or embolism, with extensive infarction of the intestine, and gangrene and death in a high percentage of cases. Again, only in recent years has there been interest in and recognition of milder forms of intra-abdominal vascular disease.

Abdominal pain or angina, which may be compared with cardiac angina and claudication of the extremities, predicates a concept of spasm of the mesenteric vessels, giving rise to ischemia of the intestinal musculature associated with pain, but without necrosis. Furthermore it could be postulated that a small infarct of the intestine could heal without perforation if only the terminal arterioles were involved and collateral circulation was adequate. This last concept to date has not been substantiated by either experimental or pathological proof, but an accumulation of some clinical data helps to uphold this theory.

In 1936 Dunphy,[1] at the Peter Bent Brigham Hospital in Boston, reviewed the case histories of 12 patients who had died from massive mesenteric thrombosis. Seven of these patients gave a history of repeated attacks of abdominal pain, previously undiagnosed, preceding the fatal attack by months and years. He reported in detail a case in which, for many months, the patient had had severe abdominal cramps occurring approximately an hour and a half after eating. This patient subsequently died from a massive mesenteric infarction. McClenahan and Fisher,[2] at the Mercy Hospital, University of Pittsburgh, reviewed 40 cases in 1948, again emphasizing the frequency of mild episodes of abdominal pain for a period preceding the massive infarction. Miller,[3] of Boston, described an extremely interesting case of a forty-five-year-old man with severe hypertension who was admitted to the hospital with a diagnosis of mesenteric thrombosis. This patient was not operated upon and recovered, but died six months later of another cause. Autopsy revealed a healed infarct in the ileum. Again, in a recent case[4] a forty-six-year-old man had recurrent episodes of abdominal pain for eight years. A subtotal gastrectomy had been performed for benign gastric ulcer, but the pain recurred periodically and progressed in severity and frequency. Two exploratory laparotomies were entirely negative, and the patient subsequently died of undiagnosed inanition. Autopsy revealed severe arteriosclerosis of the aorta and mesenteric vessels. There was an associated congenital anomaly of the mesenteric vessels, with marked hypertrophy of the superior mesenteric artery. *There was a fresh occlusion of the superior mesenteric artery with incipient gangrene of the small intestine.* Conceivably, the previous attacks of abdominal pain could have been on the basis of angina due to spasm of the mesenteric vessels, which was not demonstrable at the time of the laparotomies.

The following cases are further enlightening and give clinical support to the concept of abdominal angina.

CASE REPORTS

CASE 1. Mrs. L. R. M., a 72-year-old housekeeper, was admitted to the University Hospital on February 24, 1949. She had enjoyed apparent good health until 4 weeks before admission, when she noticed the onset of diffuse abdominal

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pain, crampy in nature, that was more severe in the left side of the abdomen. In the past week the pain had become almost periodic, and, as the patient described it, "she would have a colic" in the left side of the abdomen about 2 hours after eating. Associated with this, she noted noises and rumbling in the abdomen, with some bloating. When larger quantities of food were eaten, these symptoms became aggravated. She became anorexic owing to fear of the colic, but there was no nausea or vomiting. There was no change in bowel habits, and at no time did she describe gross bloody or tarry stools.

The patient had had hypertension for many years, the systolic pressure ranging from 200 to 250. Otherwise, the past history was entirely uneventful.

Physical examination showed a well developed and well nourished, bright, elderly woman in no acute distress who did not appear chronically ill. There was no evidence of icterus. The essential positive findings was a blood pressure of 180/100, with evidence of marked sclerosis of the peripheral vessels. The heart was moderately enlarged, the border of cardiac dullness extending to the left; there was a soft, blowing systolic murmur over the apex. The abdomen was not distended and was soft. There were no palpable organs or masses. There was moderate, generalized, left-sided, direct and rebound abdominal tenderness, with no muscle guarding. Pelvic and rectal examinations were negative. The admission diagnosis was diverticulitis or neoplasm of the large bowel.

Examination of the blood disclosed a red-cell count of 4,200,000, with a hemoglobin of 12 gm. per 100 cc. The urine was normal. The blood nonprotein nitrogen was 30 mg., and the total protein 6.4 gm. per 100 cc. A guaiac test for occult blood was slightly positive on two occasions. Barium-enema x-ray study revealed no lesion of the colon.

Under observation in the hospital the patient was afebrile. Symptomatically she improved, and in the light of the negative laboratory investigations, she was ready for discharge on the 4th hospital day. However, nausea and vomiting and increased pain and tenderness in the left side of the abdomen developed. It was deemed advisable to perform an exploratory laparotomy. A 15-cm. left-rectus-muscle-splitting incision was employed. A moderate amount of free serosanguineous fluid was found in the peritoneal cavity. There were numerous fine, flame-shaped hemorrhages in the mesentery of the middle portion of the jejunum adjacent to the bowel. In the center of this site was a 5-cm. partially organized, infarcted area of small bowel, with dimpling and contraction of the serosa, and partial narrowing of the lumen, with hemorrhagic change in the bowel wall. This appeared old and in the phase of final organization. A peristaltic wave passed over the center of this area, proximal to which there was mild dilatation of the bowel. After full exploration of all the abdominal organs it was decided to close the abdomen, since the natural repair of the infarcted area was progressing satisfactorily.

The course was quite uneventful except for transient vomiting and distention on the 2nd postoperative day. This was relieved promptly by a Levine tube and suction. The wound healed by first intention. Immediately after operation the patient was given Dicumarol therapy in an attempt to prevent any further formation or propagation of mesenteric thrombi. The prothrombin time was brought down to 20 per cent of normal by the 5th postoperative day and maintained at this level. The patient was discharged on the 13th postoperative day. She was given Dicumarol, 50 mg. daily, at home, with observation of the prothrombin time twice a week.

The patient was doing well at home, eating small meals and was free of any abdominal pains. However, 4 weeks after discharge she was readmitted to the hospital because of Dicumarol toxicity, with resulting hematuria, and rectal bleeding 24 hours before admission. The prothrombin time was 86 seconds (control, 15 seconds). Dicumarol was discontinued, and she was treated with daily doses of 72 mg. of Hykinone, and also blood transfusions. Bleeding stopped, and she was discharged 4 days later, when the prothrombin time was 75 to 80 per cent of normal.

Subsequent monthly follow-up visits in the office show the patient to have a persistent hypertension, the systolic pressure being 200 to 250. She has an occasional episode of low-grade abdominal colic coming on between meals, but otherwise she is asymptomatic. She has been advised to take small feedings at frequent intervals and to avoid large meals.

CASE 2. C. J. K., a 67-year-old lawyer, was admitted to the University Hospital for the third time on August 16, 1949.

The patient's first admission was in 1943 because of low back pain due to hypertrophic arthritis.

He was readmitted 2 weeks later for evaluation of his cardiac status in preparation for herniorrhaphy. At that time he had a history of angina pectoris for several years and a definite coronary occlusion about 4 years before. An electrocardiogram showed changes of an old posterior-wall infarct, and it was considered best not to repair the hernia.

About 5 months before admission the patient had recurrent bouts of cardiac angina. In March, 1949, he was in Syracuse Memorial Hospital for an episode of acute periumbilical pain with vomiting, which spontaneously subsided just before admission. Studies then showed negative abdominal findings, and serial electrocardiograms revealed no additional changes.

At the third admission the patient gave a history of 36 hours of recurrent, generalized abdominal, crampy pain associated with three loose bowel movements at the onset. During this interval the patient had been followed very closely by his physician, who continuously found a soft, relaxed abdomen with a low-grade tenderness in the left lower quadrant and no spasm. Four hours before admission the patient experienced persistent pain in the middle portion of the abdomen, with repeated vomiting, and he had had no bowel movements for 24 hours before admission. None of the vomitus or previous bowel movements had contained any old or fresh blood. His physician saw him again at this time and referred him to the hospital with the diagnosis of acute condition of the abdomen. There was no history of previous gall-bladder disease or peptic ulcer or of urinary difficulties.

Physical examination revealed the patient to be in moderately severe abdominal pain and quite dehydrated. The heart and lungs were normal; the abdomen showed moderate distention, particularly in the left middle portion and left lower quadrant, with marked direct and rebound tenderness, most marked in the left lower quadrant. No rigidity was present.

The temperature was 103°F., the pulse 96, and the blood pressure 150/90.

Examination of the blood disclosed a white-cell count of 11,600, with 80 per cent neutrophils. Urinalysis was negative. The blood amylase was 35 units, and the nonprotein nitrogen 35 mg. per 100 cc. A preoperative diagnosis of abdominal angina with progression to mesenteric thrombosis was made.

Transfusion was started, and the patient was taken to the operating room for laparotomy about 2 hours after admission. A 15-cm. left-rectus-muscle-splitting incision was employed. There was a moderate amount of serosanguineous free fluid in the peritoneal cavity (which was subsequently reported as negative for aerobic and anaerobic bacteria). The middle portion of the jejunum was found to be infarcted for about 15 cm., but the subtending mesentery showed no gross thromboses except for the terminal recti vessels adjacent to the bowel, which appeared dark and firm and contained thrombi. The gangrenous jejunum was resected liberally, and an end-to-end jejunojejunostomy was performed, interrupted silk for the serosa and a continuous Connell 00 chromic catgut for the anastomosis being used. Complete exploration of the remainder of the abdomen was negative.

The postoperative course was unusually uneventful. A Wangensteen tube was kept in place for 48 hours. On the 3rd postoperative day the patient had a spontaneous bowel movement. He was given immediate effective anticoagulant therapy, starting with heparin and continuing with Dicumarol. An effective level of prothrombin — between 15 and 25 per cent (Quick test) — was obtained. He had several episodes of cardiac pain, but serial electrocardiographic tracings merely showed evidence of old anteroseptal infarction and no recent progressive changes. During the end of the 1st postoperative week he complained of mild postprandial distress coming on 1 or 2 hours after eating, with dull pain and bloating. He was discharged from the hospital on the 15th postoperative day with primary wound healing. Di-

cumarol therapy was continued for a period of 6 weeks after operation. The patient was advised to take small, frequent, bland feedings and to avoid large meals.

Discussion

It is reasonable that this concept of abdominal angina could account for a large number of undiagnosed cases of abdominal pain and distress, particularly in elderly patients. Given a case of severe arteriosclerosis with hypertension and superimposed vasospasm, the resulting ischemia of the intestinal musculature could conceivably give rise to cramps or ill defined pain with bloating and dyspepsia. The ingestion of food would represent exercise for the bowel, and would be followed by these complaints one to three hours later, depending upon the segment of intestine involved. Unless the process progressed to thrombosis and infarction of the intestine, with peritoneal irritation, there would be few or no localizing symptoms or physical findings.

Fortuitously in Case 1, in which operation was done in an interval period, a healed infarct of the middle portion of the jejunum was encountered that did not require surgical excision. In the nine-month follow-up period to date there have been no recurrent severe episodes, although the patient complains of cramps and bloating two or three hours after she eats a heavy meal.

In Case 2, on the basis of the history and physical findings, a correct preoperative diagnosis of abdominal angina, progressing to mesenteric infarction, was made. In this patient, again, there was not the massive infarction seen with large-vessel closure, but, instead, infarction of a localized segment of jejunum that had progressed to necrosis because of wider involvement of the terminal mesenteric vessels and failure of collateral circulation. There have been, of course, numerous case reports of massive infarction of the small intestine due to closure of the main vessels, with successful resection. These cases represent a more extensive form of the disease with involvement of larger mesenteric vessels. This type of case, which has been more widely recognized and reported, has overshadowed the less severe forms and would be analogous to myocardial infarction as against angina pectoris as represented by abdominal angina.

Summary

An attempt is made to uphold the analogy between intra-abdominal vascular disease and disease of the vessels of the heart and extremities, giving rise to angina and claudication.

Cases from the literature that tend to substantiate this clinical concept are discussed.

Two new cases demonstrating involvement of the smaller mesenteric vessels are reported — the first with a healed infarction demonstrated at exploratory laparotomy, and the second with a localized segment of infarction and necrosis of intestine requiring resection. In both cases so-called abdominal angina seemed to fit the pathological picture.

References

1. Dunphy, J. E. Abdominal pain of vascular origin. *Am. J. M. Sc.* **192**: 109-113, 1936.
2. McClenahan, J. E., and Fisher, B. Mesenteric thrombosis. *Surgery* **23**:779-785, 1948.
3. Miller, R. H., Cushman, G. F., and Kilgore, A. R. Syndrome of mesenteric or subperitoneal hemorrhage (abdominal apoplexy). *Ann. Surg.* **114**:672-681, 1941.
4. Case Records of the Massachusetts General Hospital (Case 35071). *New Eng. J. Med.* **240**:262-267, 1949.

ANTIRHEUMATIC ACTIVITY OF ASCORBIC ACID IN LARGE DOSES*

Preliminary Observations on Seven Patients with Rheumatic Fever

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THE purpose of this paper is to present observations suggesting that ascorbic acid possesses antirheumatic activity when administered in large doses. Because of the small number of patients treated so far, the relatively short period of follow-up study and the well known variability of rheumatic fever even when it is uninfluenced by therapy, the present communication must be considered preliminary in the strictest sense of the word. Nevertheless, the apparent responses of a group of 7 patients treated within the past three months have been sufficiently impressive to warrant this report.

OBSERVATIONS

Since January 2, 1950, ascorbic acid|| has been given by mouth in doses of 1 gm. four times daily (total of 4 gm. per day) for periods varying from eight to twenty-six days to a total of 7 patients with rheumatic fever. There has been a follow-up period of twelve days to two months in 3 patients in whom therapy has been discontinued; at the time of this writing, March 20, 1950, 4 patients are still receiving treatment.

The results of treatment with ascorbic acid can best be presented by a brief description of the clinical course of each of the 7 patients:

CASE 1. P. L. is a 13-year-old boy whose pertinent findings prior to treatment included migratory polyarthritis, a temperature of 101° to 102° F. by rectum and elevation of the sedimentation rate. His heart seemed normal except for a slight systolic murmur. Ascorbic acid was given for a total of 8 days (January 2 through January 9, 1950). Within 24 hours of the beginning of treatment the joint manifestations had disappeared, and the fever had lessened. The temperature remained normal after the 2nd day of therapy, but the sedimentation rate continued to be elevated.

CASE 2. R. M. is a 14-year-old boy who has suffered for many months from persistent rheumatic fever, severe cardiac involvement and chronic hepatic congestion. Ascorbic acid therapy was begun on February 4, 1950, during a period of increasing rheumatic activity (possibly just a rheumatic-fever cycle), manifested by temperature elevation to 102°F. by rectum, rise in the sedimentation rate and increased congestion of the liver. The fever began to lessen on February 5, and the temperature has remained normal since February 6. The size of the liver has not changed appreciably, and the sedimentation rate is still elevated. Ascorbic acid was given for a total of only 8 days.

CASE 3. E. T. is a 15-year-old boy who for 6 weeks prior to therapy had been ill with migratory objective polyarthritis, fever, sinus tachycardia and a rapid sedimentation rate. Except for a slight systolic murmur, his heart seemed normal. With ascorbic acid therapy, which was given for a total of 15 days (February 21 to March 7, 1950), there was prompt improvement in symptoms and reduction in fever. Since the 2nd day of treatment the temperature has been entirely normal, and there have been no symptoms or signs referable to the joints. By March 20 the sedimentation rate had fallen to within normal limits.

CASE 4. W. D. is a 14-year-old boy with rheumatic heart disease whose symptoms of rheumatic fever had been controlled by acetyl salicylic acid. However, after the omission of this drug and prior to treatment with ascorbic acid he had elevation of the temperature to 102°F. by rectum, several nosebleeds and a swollen painful knee. Ascorbic acid therapy was begun on February 22, 1950, and continued to the present time. Improvement was definite but gradual over a 4-day period. He has been symptom-free and afebrile since February 26. The sedimentation rate has fallen from an initial level of 1.4 to the slightly elevated level of 0.55 mm. per minute.

CASE 5. R. F. is an 11-year-old girl who, on admission to the hospital on March 6, 1950, was obviously acutely ill with active rheumatic fever, pancarditis and congestive heart failure. Pertinent findings included a temperature of 104°F. by rectum, tender, swollen finger joints, a respiratory rate of 60 to 75, cardiac enlargement, murmurs of mitral regurgitation and aortic regurgitation, nodal rhythm, a ventricular rate of 160, a pericardial friction rub, marked enlargement and tenderness of the liver, and edema of the legs and lower back. Treatment with ascorbic acid was begun on the evening of March 6. The fever and joint symptoms gradually lessened and have been completely absent since March 13. The friction rub has not been audible since March 10. The cardiac rhythm reverted to normal within 24 hours of therapy, and the heart rate is now about 120. Hepatic congestion and peripheral edema have entirely disappeared. The patient now feels well and appears obviously much improved. The sedimentation rate is still elevated.

CASE 6. A. F. is an 18-year-old boy without cardiac involvement whose rheumatic-fever manifestations just prior to ascorbic acid therapy (given from March 7, 1950, to the present) consisted of elevation of the temperature to 101°F. by rectum, objective polyarthritis and elevation of the sedimentation rate. Treatment was followed by somewhat slow but steady improvement. The temperature has been normal since March 10, and the joint manifestations have remained completely subsided since March 11. The sedimentation rate is still elevated.

CASE 7. P. B. is a 5-year-old boy with known rheumatic heart disease who had a recrudescence of rheumatic fever on March 9, 1950. Manifestations included elevation of the temperature to 104°F. by rectum, sinus tachycardia, pallor and pain and tenderness of the right knee and both ankles.

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||The ascorbic acid for this study was supplied by Hoffmann-LaRoche, Incorporated, Nutley, New Jersey.

The joint symptoms subsided spontaneously prior to treatment, but the high fever continued. Ascorbic acid therapy was begun on March 14. Since that time there has been a steady decline in temperature, and fever has been entirely absent since March 17. The heart rate has slowed, and the patient's appearance has greatly improved.

Discussion

In 1933 Rinehart[1] proposed the concept that vitamin C deficiency may play a role in the etiology of rheumatic fever, and since that time he and many other investigators have studied the metabolism of ascorbic acid in rheumatic fever and arthritis and have attempted to use it in the treatment of these diseases. However, as far as we are aware, a beneficial effect of ascorbic acid on the course of active rheumatic fever has hitherto not been demonstrated. These previous therapeutic failures may perhaps be attributed to the fact that practically all investigators were thinking in terms of vitamin C deficiency and, hence, used doses of ascorbic acid considerably smaller than those used by us.

Although ascorbic acid is generally considered innocuous, and although no untoward reactions have been encountered in the course of our limited observations, there is obviously a need for careful toxicity studies. It is possible that individual doses of more than 1 gm. or total daily doses of more than 4 gm., if found harmless, may prove to be therapeutically even more effective.

The mechanism by which ascorbic acid may influence the rheumatic process is not known, but the large amounts required to produce the apparent effect suggest that it is not a simple matter of replacement therapy. The relation of ascorbic acid to the activity of the adrenal cortex[2] and the recently demonstrated value of adrenocortical activity in the treatment of rheumatic diseases[3-5] raise many interesting questions concerning the problem of mechanism that cannot be discussed in this short report.

Finally, it should be emphasized that, although our observations suggest that ascorbic acid when administered in sufficient amounts possesses antirheumatic activity, no final assessments can yet be made regarding the possible therapeutic value of this substance. Data are as yet insufficient to allow for a comparison of ascorbic acid with salicylates, cortisone, ACTH and other antirheumatic agents. Nevertheless, this preliminary report is offered, to stimulate further investigations of the therapeutic potentialities of ascorbic acid, of its relation to the antirheumatic action of adrenal hormones and of its possible local role in the tissue reactions that we call rheumatic fever. It also indicates the need for caution in interpreting apparent antirheumatic effects obtained from combinations of various hormones and ascorbic acid.[6]

Summary

Observations suggesting that ascorbic acid in doses of 4 gm. daily possesses antirheumatic activity are presented.

The possible significance of these observations is briefly discussed, and the need for extending them is emphasized.

We are indebted to Drs. George Sturgis, Joseph Knobloch, Royal Schaaf and Susan Butler for their help in the clinical supervision of the patients.

References

1. Rinehart, J. F., and Mettier, S. R. Joints in experimental scurvy and in scurvy with superimposed infection. With consideration of possible relation of scurvy to rheumatic fever. *Am. J. Path.* **9**:952-955, 1933.
2. Sayers, G., and Sayers, M. A. Pituitary-adrenal system. *Ann. New York Acad. Sc.* **50**:522-539, 1949.
3. Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F. Effect of hormone of adrenal cortex (17-hydroxy-11-dehydrocorticosterone: compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis: preliminary report. *Proc. Staff Meet., Mayo Clin.* **24**:181-197, 1949.
4. Hench, P. S., et al. Effects of adrenal cortical hormone 17-hydroxy-11-dehydrocorticosterone (Compound E) on acute phase of rheumatic fever: preliminary report. *Proc. Staff Meet., Mayo Clin.* **24**:277-297, 1949.
5. Massell, B. F., Warren, J. E., Sturgis, G. P., Hall, B., and Craige, E. Clinical response of rheumatic fever and acute carditis to ACTH. *New Eng. J. Med.* (in press).
6. Lenin, E., and Wassen, E. Effect of combined injections of deoxycortone acetate and ascorbic acid on rheumatoid arthritis. *Lancet* **2**: 993, 1949.

WHY I AM IN FAVOR OF COMPULSORY HEALTH INSURANCE

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THE Committee on the Costs of Medical Care[1] demonstrated in 1932 important problems in the delivery of medical care in the United States. The Committee disagreed on the best method to solve them. In 1937 the American Foundation's report[2] confirmed these problems. About 1942 the rejections by Selective Service emphasized the lack of medical care for certain citizens in a particular age group. Unfortunately, discussion about these figures has not clarified the subject. Both President Roosevelt and President Truman have urged improvement in the delivery of medical care. The bills related to medical care before the Congress today and the interest shown in the subject by the public at large prove that problems are still unsolved.

The term "socialized medicine," often used in a derogatory sense, has added confusion. Of course, the term does not express an entity. A very good definition of socialized medicine has been offered by Dr. Paul R. Hawley, chief executive officer of the Blue Cross–Blue Shield Commissions: "I would define 'socialized medicine' as medical care supported in whole or in large part by tax money and regulated by government." One must realize that according to this definition socialized medicine already exists in this country and offers individual care to millions of citizens. Therefore, the opponents really are only opposed to the extension of existing socialized medicine for which the Administration's bill calls.

Especially since 1932 proposals to solve the problems of the delivery of good medical care have been presented by organized medicine and others, both within and without the profession. The majority votes of organized medicine, whether at the national, state or local level, have usually opposed the proposals by minority groups in the profession or by laymen. Interestingly enough, these majorities have over the years repeatedly changed their attitude in regard to such proposals. Examples are the opposition to Blue Cross and Blue Shield plans, group practice and prepayment plans organized by laymen and co-operatives. Possibly, the original judgments of the majorities in organized medicine have been too reactionary, which suggests that organized medicine's opposition to President Truman's National Health Program may also be ill conceived.

Among the problems, two important ones arouse the most discussion — namely, how to pay for the justifiably high cost of good care and how to eliminate charity medicine and the much disliked "means test" for those who are not actually indigent. The raising of sufficient funds is the real answer to these problems. Organized medicine hopes to raise the funds by voluntary prepaid nonprofit insurance plans supplemented by taxes as collected today. S. 1679, the Administration bill at present before Congress, plans to raise the funds through a new form of taxation called compulsory health insurance, supplemented by general tax funds if necessary. Under this method practically everyone, except the actually indigent, would be contributing to the health fund, and, therefore, would have a right to noncharity medical care.

I consider the philosophy behind S. 1679 the better, for despite the extraordinary growth of Blue Cross and Blue Shield plans over the past twelve years they have failed to offer comprehensive medical care because of insufficient funds raised on a voluntary basis. Furthermore, they have not eliminated self-medication and drug-clerk diagnosis and treatment so frequently used, owing, in my opinion, to the lack of inclusion of preventive medical procedures and early diagnosis without extra charge in their contracts. Also, they have not diminished the number of people who have to accept charity medicine and to be subjected to the "means test," if one can judge from the attendance at charity clinics. These plans controlled by organized medicine have also failed to develop standards to guarantee good quality of care. For organized medicine has never seen fit to limit the activities of its members to what they are qualified to do.

On the other hand, the program in S. 1679 can raise sufficient funds to provide for comprehensive medical care guided by the physician of one's choice. It also encourages preventive medicine and early diagnosis. It eliminates charity medicine and the means test for all, except the actually indigent. It makes the opportunity for medical care, like education, the right of all people. With the dollar barrier eliminated between the patient and the physician the dangerous procedures — done in the spirit of economy — of self-medication, drug-clerk diagnosis and therapy and so forth should markedly diminish. Furthermore, the plan calls for lay control in the development of rules to guarantee quality. Experience has shown that lay boards of trustees of hospitals have developed better rules to guarantee higher quality care than organized medicine has

Therefore, I believe not only that under S. 1679 sufficient funds can be developed, which voluntary plans so far have failed to do, to solve the two important problems mentioned above but also that better rules will be developed to guarantee a good quality of medical care.

*Chairman, Committee for the Nation's Health.

REFERENCES

1. Committee on the Costs of Medical Care. *Medical Care for the American People.* 213 pp. Chicago: University of Chicago Press 1932.
2. American Foundation. *American Medicine: Expert testimony out of court.* 2 vol. 1500 pp. New York: The Foundation, 1937.

WHY I AM OPPOSED TO COMPULSORY HEALTH INSURANCE

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IN CONSIDERING the pros and cons of a health insurance program, the needs to be met by such a program must be clearly established. These needs may be briefly stated as follows:

Better medical care for all the people should be provided, including better preventive, diagnostic and curative medicine. This requires better trained physicians and better facilities for their work. Neither of these requirements will be met unless there is created and maintained in the physicians themselves a continuing desire to improve their own capabilities and to bring to their patients, at all times, more of the increasing knowledge in matters of health and disease. The incentive for improvement and for the industrious application of this skill must be encouraged.

A better mechanism of payment for medical care must be developed. Our chief concern in this matter is with the large segment of the population that is making a decent living, with standards higher than those in a comparable group of any large country in the world, and is still not financially able to meet the costs of serious illness when it strikes.

Compulsory health insurance is proposed as a mechanism of paying for medical care. This may best be discussed in three important aspects.

First is the *quality of the care provided*. Wherever compulsory health coverage has been adopted, the emphasis soon comes to be placed on *quantity*, not *quality* of care. In 30 per cent of the last fifty patients who were referred to me for treatment of cancer of the large bowel, the physician failed to make an early diagnosis because of inadequate history or superficial examination. The diagnosis of obscure conditions means time and thoughtful concentration upon each individual problem. This opportunity will be lost under a compulsory system, because "free" medical care to all means more unnecessary visits to the doctor by many. The complaining patient with no disease will demand more time than the patient with few symptoms but with serious disease. This leveling-off process stimulates superficial and careless examinations and poorer, rather than better, quality of care at the level of the family practitioner, where early diagnosis should be made.

Medical care of high quality demands active participation by the physicians of each community in a continuing training program, and their availability individually or collectively, at all times, day and night through the year. Doctors are normal people trained along special lines. They rank high in community spirit, but it is unrealistic to depend upon the high calling of the doctor to create the incentive for these efforts. A feeling of responsibility to the individual and the knowledge that personal efforts will be rewarded in one way or another in proportion to the efforts expended are essential, and will not come from a system of medical care that puts its emphasis on quantity.

Simons and Sinai,† in discussing *preventive medicine* as an all-important aspect of medical care, say: "At no point has a disappointment been greater than in the failure of insurance as a preventive measure."

Second is the *cost*. A completely comprehensive medical care program is not insurable because of the cost, which is unpredictable and cannot possibly be paid for out of payroll deductions. Compulsory health insurance, in other words, is not insurance but is a form of taxation.

It costs the Government $20,000 to $51,000 per bed to construct a hospital in areas where voluntary organizations do the same for $16,000. The length of hospital stay following various operations in the Veterans Administration hospitals is, moreover, from two to six times as long as that in voluntary general hospitals, with all the extra expense involved. More money, however, does not mean better care. The care that a patient receives can only be so good, regardless of the amount of money that is invested in it. We want all the care that anybody needs, but under a financial structure that makes it efficient and effective, not extravagant in cost.

Third is the need for careful *experimentation* before adopting a complete change in our program of medical care. There is lacking in this country today both the experience and the knowledge necessary to write a compulsory program to cover the needs of the country, nor is it possible at the present time to create immediately an effective voluntary program that will fulfill these needs. What is needed is experimentation toward the end that our objectives may be reached. All the initiative and energy that can be mustered are essential if a satisfactory program is to be worked out in the near future. If a compulsory health insurance program is put into effect tomorrow, all experimentation stops except within the structure of that program — all voluntary plans will disappear, and the initiative and efforts so essential for a sound program will be wanting because the responsibility is no longer ours but belongs to the federal Government. The effects of such a system have been well expressed by the International Labor Office as follows:

> Once the whole employed population, wives and children included, is brought within the scope of Compulsory Sickness Insurance, the great majority of doctors, dentists, nurses and hospitals find themselves engaged in the Insurance Medical Service which squeezes out most of the private practice on the one hand and most of the medical care heretofore given by public authorities on the other. The next step to a single national medical service is a short one.

*President-elect, Massachusetts Medical Society.

†Simons, A. M., and Sinai, N. *Way of Health Insurance.* 215 pp. Chicago: University of Chicago Press, 1932. P. 156.

MEDICAL PROGRESS

SOME NEW PATHOLOGICAL CONCEPTS*

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PATENTLY it is impossible to review the entire subject of progress in pathology for the past few years. As in all fields of endeavor that have come of age, the further increments of knowledge that have been achieved in pathology have been concerned chiefly with expanding and correlating already existing knowledge. Thus, the past few years have seen no startling discoveries but rather detailed study and expansion of pre-existing observations. This communication attempts to indicate briefly some of the trends in the recent literature and then to consider in greater detail certain specific areas in which significant progress has recently been reported.

For many years pathologists and clinicians alike have tended to divide their concepts of disease into compartments. Ulcerative colitis has long been considered as a pathologic entity involving essentially the colon alone, and one thinks of hepatitis as a dysfunction solely of the liver. However, within the past few years the trend has been away from this segmental conception. The recent literature has stressed the view that most diseases, regardless of their particular point of attack, tend to affect the body as a whole. In line with this concept, careful pathological examination of all organs in many conditions has revealed many hitherto unobserved correlated changes. Increasing numbers of references are seen to renal changes in liver disease, liver and renal changes in gastrointestinal disease and similar relations. A few citations of these recent reports will suffice to document this newly developed interest.

Baxter and Ashworth,[1] in 1946, recalled attention to the occurrence of renal disease in cases of cirrhosis of the liver. These changes occurred in cases without jaundice and therefore were distinct from so-called bile or cholemic nephrosis. Histologically, no bile pigment was present in the kidney, and the essential features described were those of tubular epithelial degeneration. Some of the changes were not entirely definite. However, at least in some of the cases cited, unmistakable fatty degeneration of the renal tubular epithelium occurred. Corroboration of these observations has been made in occasional cases of cirrhosis of the liver seen at the Mallory Institute of Pathology. These examples of renal tubular epithelial degeneration were found mostly in Laënnec's cirrhosis and consisted essentially of fatty degeneration of the proximal convoluted tubules. Since present-day thinking is largely agreed that this type of cirrhosis is probably nutritional in origin, toxic factors affecting simultaneously the liver and kidney can be ruled out as producing the renal lesion. It has not yet been established whether this type of renal damage may occur in other forms of cirrhosis. Since the liver lesion appears histologically to be considerably older than the renal lesions, it may be involved in the production of the kidney lesion.

Renal dysfunction has been cited as occurring in infectious hepatitis.[2] Thus, the much discussed hepatorenal syndrome, which has for so long been a somewhat ephemeral entity, appears to be gaining some possible anatomic foundation.

Turning to pathologic entities that affect chiefly the gastrointestinal tract, many cases of ulcerative colitis are found at autopsy to be associated with fatty metamorphosis of the liver and occasionally with cirrhosis of that organ. The possibility that these changes are merely coincidental has not yet been ruled out, although the likelihood is strong that some correlation exists. This ulceroinflammatory disease of the colon has also been shown to be associated with changes in the kidney.[3] Here again these changes are parenchymal. In the kidney vacuolation of the epithelium of the proximal convoluted tubules, so-called hydropic vacuolation, occurs. These vacuoles are free of fat, glycogen and pigments and appear to contain fluid. The genesis of these lesions is obscure, as is their relation to ulcerative disease of the colon. It is possible that the renal changes represent a response to the noxious agents that likewise affect the bowel. On the other hand, it is equally possible, and perhaps more probable, that the kidney and liver lesions result from the metabolic imbalances, anemia and sepsis incident to the ulcerative lesions in the colon. The clinical significance of these related lesions is as yet not established. In several cases of ulcerative colitis evidences of impaired renal function were present, occurring for the most part late in the course of these fatal cases.[3] However, so many factors are present in these critically ill patients that could possibly have altered the kidney function that it is impossible to ascribe any definite im-

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portance to any specific renal anatomic lesion. Future renal-function studies on patients with ulcerative colitis may shed some light on the significance of these tubular changes.

These brief references are intended only to illustrate the recent trends occurring in pathology. A few specific fields, listed below, in which significant progress has lately been achieved are considered in detail: infectious mononucleosis, so-called "lateral aberrant thyroid tumors," the status of carcinoma in situ, with particular reference to cervical carcinoma, the relation of pigmented moles to malignant melanoma and the pathology of shock.

Infectious Mononucleosis

Infectious mononucleosis, the so-called "medical students'" disease, with its splenomegaly, lymphadenopathy and abnormal lymphocytosis, frequently simulates more serious disorders such as leukemia. When the diagnosis of infectious mononucleosis is established in any case, therefore, it invariably brings with it considerable comfort to the physician and relief to the patient. The mortality is exceedingly low. In general, the prevailing medical attitude has been that the entity was more of a nuisance than a menace. In the light of present knowledge this attitude requires certain alterations. Possible rupture of the spleen in the course of this disease has recently received considerable attention in the literature. At the same time an increasing awareness of liver complications has appeared. Cutaneous lesions and cerebral symptoms have been described, and the entire concept and significance of the disease have become greatly expanded. Because of the rarity of uncomplicated deaths in this entity, little has been known of its pathology except for some studies on the lymph nodes and spleen. Only in the recent past have any significant post-mortem studies been made. The first autopsied cases were described in 1939 by Thomsen and Vimtrup.[4] This pioneer report was followed by scattered liver-biopsy studies on patients with hepatic dysfunction.[5, 6] Additional isolated autopsied cases were reported, and today the total number of cases barely exceeds a dozen (Custer and Smith[7]).

These pathological studies have all emphasized one point. Infectious mononucleosis is a widespread systemic disease having the potentiality of producing considerable morbidity and even mortality. It involves virtually every tissue in the body. The sites of major involvement are the lymphatic and hematopoietic systems. The lymph nodes are invariably enlarged, usually having prominent follicles, reticuloendothelial and lymphatic hyperplasia, as well as diffuse infiltration with atypical lymphocytes — the so-called infectious-mononucleosis cell. The spleen likewise has long been known to be enlarged. Here again the follicles show enlargement. They are sometimes obscured by the flooding of the architecture with lymphoid and mononuclear elements. The capsule, trabeculae and sinusoidal walls show similar infiltration. The same cells, typical and atypical lymphocytes, are found in the sinuses and pulp spaces. The heart, lungs, kidneys, digestive tract and adrenal and pituitary glands, as well as the brain, show focal infiltrates. These infiltrative cells, disposed chiefly perivascularly in collar fashion, are largely lymphoid forms with occasional so-called infectious-mononucleosis cells. The liver has been shown to be an important site of disease, presenting a very varied pattern. For many years the icterus associated with mononucleosis was ascribed to partial obstruction of the excretory biliary system by enlarged porta-hepatis lymph nodes. The Scandinavian workers soon discredited this theory by the direct expedient of liver-biopsy studies.[6] Hepatitis was plainly evident, focal in character, with lymphoid aggregates about the portal areas and rare necrosis of individual cells associated with other areas of regeneration. Of great interest, however, is the fact that these changes have been observed in patients without clinical jaundice as well as in those with apparent hepatic dysfunction. Liver involvement, demonstrable by liver-function studies or tissue studies, or both, has been proved to be a very common if not an invariable feature of mononucleosis.[8] Peterson[8] shows that the degree of impairment of function may be so severe as to make the differential diagnosis between mononucleosis and infectious hepatitis extremely difficult. In a case seen at the Mallory Institute of Pathology the degree of hepatic damage was sufficiently marked to reproduce histologically the changes seen in severe cases of infectious hepatitis. Widespread hepatocellular damage was evident. Considerable distortion of the hepatic lobular architecture was present. Although only widely scattered necrotic cells were present, innumerable mitotic figures and multinucleate atypical cells attested to an active regenerative process. As one would expect from these histologic studies, sporadic cases of infectious mononucleosis have been observed in which the presenting predominating feature of the case has been liver disease alone. It hardly requires mention, therefore, that atypical cases of apparent hepatitis may indeed be instances of infectious mononucleosis. The heterophil-antibody test permits the separation of these similar entities since, to the best of my knowledge, it is not positive in infectious hepatitis.

It is therefore apparent from the studies mentioned above that earlier concepts about the insignificance of infectious mononucleosis deserve revision in the light of present pathological and clinical knowledge. In addition to the liver changes described, marked splenomegaly is of considerable importance, since rupture of this organ has caused death in certain cases. Indeed, rupture of the spleen

with severe, even fatal, hemorrhage may be the first and only symptom of the disease.[9, 10] Nasopharyngeal hemorrhage from hyperplastic lymphoid tissue, myocarditis and central respiratory paralysis have all been cited as causes of death. It appears, therefore, that infectious mononucleosis is associated with a much more widespread tissue involvement than was formerly appreciated, producing a morbidity and mortality meriting careful attention.

Lateral Aberrant Thyroid Tumors

The subject of tumors of the thyroid gland has long been one of the most controversial in pathology. The widely divergent views that emanate from various pathological laboratories concerning the frequency of these tumors and their relative malignancy create great confusion in the minds of most physicians. This confusion, attested to by the voluminous literature on this subject, is not without cause. The histologic criteria applied to tumors of the thyroid gland vary widely from one laboratory to another. Thus, a tumor called malignant by one pathologist may be termed benign by another pathologist using a different set of criteria. Superimposed upon this difficulty is the fact that the anatomic changes found in these tumors are frequently of the most subtle type, providing ample room for differences of opinion. And finally, as is so well known, the paradoxic clinical course pursued by these lesions contributes heavily to the complication inherent in clinicopathological correlation. In all probability, much of the bizarre behavior of these tumors has resulted from the use of traditional five-year follow-up periods of study of the cases. A recent article by Frazell and Foote[11] shows clearly the uselessness of five-year clinical follow-up studies on these patients. Many forms of thyroid cancer untreated are consistent with survival periods of ten and fifteen years. When viewed from the standpoint of more prolonged, exhaustive case study, some of the apparently bizarre behavior of these tumors is seen to be simply the result of this insufficient study.

Tumors arising in so-called "lateral" aberrant thyroid tissue have long represented a focal point of disagreement in this field. It has been believed that these neoplasms arise in displaced embryologic rests of thyroid tissue, lateral to the sternocleidomastoid muscle, and that therefore they arise entirely independent of the thyroid gland.

Opinion today has swung away from this concept. It has been established on fairly firm grounds that these so-called "lateral" aberrant thyroid tumors are in reality metastases to regional lymph nodes from a primary tumor within the thyroid gland.[12-15] This conclusion is obviously of great practical significance since it dictates the need for treating the cases as primary thyroidal cancer metastatic to regional lymph nodes.

What is the basis of this present-day concept? To begin with, in human beings considerable doubt has been thrown on the very existence of true lateral aberrant thyroid tissue — that is, tissue lateral to the carotid sheath. Gruber[16] classified these ectopic masses of thyroid tissue and used the term "lateral" to refer to structures lateral to the *thyroid* gland. However, all the masses were in reality *medial* to the carotid sheath. They therefore did not conform to the distribution of present-day "lateral masses," which are almost invariably described as being *lateral* to the carotid sheath. Dissections by King and Pemberton[12] in several thousand cases demonstrate that in man it is highly unlikely that normal thyroid tissue is ever found lateral to the carotid sheath. Moreover, examination of the recorded cases of lateral aberrant thyroid tumors discloses a more than coincidental similarity between the locations of these lateral tumors and the known anatomic sites of cervical lymph nodes. This similarity of anatomic distribution is closely tied up with the histologic observations that many of these lateral masses contain considerable lymphoid tissue in addition to thyroid tissue. It is, of course, well known that the diseased thyroid gland may contain much lymphoid infiltration. However, careful examination usually reveals that many of these lateral tumors have not only lymphoid follicles but also sinuses and, in fact, underlying lymph-node architecture.[14]

The final and seemingly conclusive proof that these tumors are in reality primary thyroid neoplasms with metastases to regional lymph nodes comes from the growing list of carefully studied cases in which primary tumors are found in the thyroid gland in virtually every case of lateral tumors. Warren and Feldman[14] analyzed a total of 57 cases of so-called lateral aberrant thyroid tumors. In 8 cases the thyroid gland was not available for analysis. In the remaining 49 cases (*all those with adequate material for study*) there was associated cancer in the thyroid gland. Wozencraft et al.[15] similarly report 3 cases in which minute primary foci within the gland were found in each, requiring study of 195 blocks of tissue in 1 case. It is important, therefore, to note that these primary sites, invariably occurring within the thyroid gland on the same side as the metastatic nodules, may be extremely small. Consequently, they are frequently not palpable, even when the gland is exposed surgically. Hence the absence of a gross tumor in cases of lateral thyroid masses has no significance in ruling out such primary foci. The finding of these primary tumors in virtually 100 per cent of the cases results only from painstaking histologic study.

This type of primary cancer of the thyroid gland is extremely slowly growing and metastasizes usually only to local lymph nodes. Many cases of long survival are on record, despite the fact that the primary

site had not been excised.[3] However, since these cases occur in relatively young patients with long expectancy of life and since these tumors have been known to cause death by widespread metastasis, it seems requisite that the clinician look upon these "lateral" aberrant tumors as metastatic foci of a malignant lesion, requiring early and adequate treatment.

Carcinoma in Situ

The term carcinoma in situ is without doubt one of the most misused terms in medicine. Pathologists themselves frequently fail to agree about its exact meaning. However, to most histologists it refers to an epithelial tumor limited to an intraepithelial situation. By definition, therefore, these tumors must not extend through the basement membrane of the epithelium. They are thus not invasive. Much of the confusion about the meaning of this term arises out of the difficulty in histologic diagnosis. The absence of invasiveness takes away from the entity the single most diagnostic feature of cancer. Moreover, from the standpoint of arriving at this diagnosis, the pathologist is at the mercy of the site from which the biopsy is taken. A strategically or fortuitously selected peripheral biopsy of a grossly invasive fungating tumor may demonstrate on that given fragment of tissue a cancer limited to an intraepithelial site. Obviously the diagnosis of carcinoma in situ in such a case, although perhaps warranted by the histologic preparation, totally ignores and distorts the true clinical picture. That such a set of circumstances may also arise in smaller tumors that are invasive in only one small focal area is even more readily understood. This difficulty in diagnosis has considerable importance since frequently the only tissue received by the pathologist is a small specimen whose site of origin is completely obscure. The relation of this biopsy to possible adjacent tumor may not be known. Hence, as TeLinde[17] has stated, when this diagnosis of carcinoma in situ is made, it remains for the clinician to fit this fragment of information into the case as a whole, to decide whether he is dealing with a true intraepithelial cancer or a peripheral biopsy of an invasive carcinoma.

Quite apart from the meaning of this term is the problem of its exact significance. What is the relation of carcinoma in situ to frank invasive carcinoma? Does it represent an early stage in the life history of carcinoma?

Most concepts about this entity have been in a state of flux for many years. However, at present there is sufficient evidence to justify the conclusion that carcinoma in situ is an early stage of invasive carcinoma.

The best studied prototype of this in situ lesion is found in the cervix. This organ is a readily accessible structure subject to relatively frequent involvement with carcinoma, permitting multiple biopsies. It is therefore ideal for this type of study.

Several recent reports on this subject demand attention.[18-21] To establish the validity of the concept that carcinoma in situ of the cervix represents an early stage of invasive carcinoma, Younge, Hertig and Armstrong[20] postulate three requirements:

> (1) Does the disease (carcinoma-in-situ) occur at a regular rate consistent with the incidence of undoubted carcinoma of the cervix?
>
> (2) Is the average age incidence consistently less than that for invasive carcinoma?
>
> (3) Is the disease an irreversible process?

Considerable information pertinent to these questions is now at hand.

At the Free Hospital for Women, Brookline, Massachusetts, it is reported that the incidence of carcinoma in situ in all cervixes studied is approximately 1.2 per cent.[20] It is important to note that this incidence results only from a routine biopsy of all diseased, *but apparently benign*, cervixes seen at this hospital, as well as also from a routine meticulous study of all cervixes removed for other causes. There is complete agreement among all well trained gynecologists that these in situ lesions are entirely unapparent clinically — a point of great importance — and that only a routine method of study, such as that detailed above, will unearth these cases. Compared with the 1.2 per cent incidence of in situ carcinomas is the 1.6 per cent incidence of frank carcinoma reported by Meigs.[22] The close similarity of these rates is at once obvious and suggests a possible close correlation between the two lesions.

Regarding the average age incidence of carcinoma in situ of the cervix, TeLinde and Galvin,[21] as well as Younge, Hertig and Armstrong,[20] agree that the patient with carcinoma in situ is approximately ten years younger than the patient with obvious carcinoma. This age difference is most noteworthy and permits only one conclusion: if carcinoma in situ does in truth progress to the undoubted cervical carcinoma it requires ten years to become a frankly invasive tumor. Many important considerations stem from this observation. To begin with, it must follow that this type of cancer is relatively slowly growing, with a long period of latency. Immediate treatment of a radical nature in this condition is injudicious and unnecessary. It must be realized that the diagnosis of carcinoma in situ rests upon very subtle histologic changes. As has been emphasized before, the cardinal diagnostic feature of malignant degeneration is absent. The diagnostic criteria therefore consist only of cellular dysplasia and anaplasia, hyperchromaticity with epithelial thickening and abnormally placed mitoses. Inflammatory changes may on occasion closely simulate these subtle variations, and it is not uncommon for competent pathologists to dis-

agree on the diagnosis. In consequence, it has repeatedly been emphasized that conservative, local therapy with close follow-up study for sufficient time to permit the establishment of the diagnosis on solid grounds is the best course to follow. It has been stated that in the absence of stromal invasion study for months, or even a year, does not jeopardize the patient and permits the clarification of the issue.

The third and most important postulate to be satisfied concerns the irreversibility of the lesion. Will it progress to carcinoma? To date 18 cases are cited by Younge et al.[20] as having passed through the stage of an intraepithelial lesion to become undoubted cases of invasive neoplasm. These cases, together with the obvious extension with time of all the other cases studied, leave no doubt about the significance of carcinoma in situ.

It can be concluded from the above evidence that carcinoma in situ in the cervix represents the beginning of an eventually invasive frank cancer. These studies have shed considerable light on the life history of cancer. At least as it concerns the cervix, it is much like the proverbial iceberg — nine-tenths hidden. These investigations open to the clinician an excellent opportunity for the detection of cancer at a curable stage and dictate the need of biopsy or cytologic study of all diseased but apparently benign cervixes.

Melanomas

An article by Allen,[23] which appeared early in 1949, represents one of the most impressive attempts to date to re-evaluate present knowledge of cutaneous nevi and melanomas. There is probably no more common tumor in man than the nevus and probably no more poorly understood tumor from the standpoint of its treatment. Contrary to the present academic point of view, Allen contends that the malignant melanoma and the benign counterpart from which it arises are both derived from epidermal cells. This view, although not new, is in direct opposition to the time-honored thesis of the neural origin of these lesions, propounded so ably by Masson,[24] among others. This epidermogenetic origin of malignant melanomas has considerable importance. If the lesions arise from the epidermis, they therefore do not arise from the malignant transformation of the cells of the simple common mole or intradermal nevus. In fact, these simple moles per se rarely, if ever, give origin to melanocarcinoma. Although this statement may seem somewhat extreme, it obviously requires a definition of the term simple mole. Are there other types of moles? It is not too widely appreciated that there are several types of moles or nevi, all having varying significances with relation to possible malignant degeneration. Totally excluding vascular and sebaceous blemishes, Allen lists five types of nevi: intradermal nevus, junctional nevus, compound nevus, juvenile melanoma and blue nevus. These five varieties are considered individually.

Intradermal Nevus

The intradermal nevus or neuronevus represents the ordinary mole found in varying numbers on virtually everyone. They are usually present from birth and are distributed over the skin of the entire body, with certain notable exceptions. They rarely occur on the palmar aspect of the hand and fingers, the soles of the feet and the scrotal sac. They may be very pale brown red to varying shades of mahogany brown and occur as either wart-like projections or flat macules. Hair is an inconstant feature; however, when it is present it almost invariably indicates this variety of mole. Histologically, the pattern is quite constant, consisting essentially of a somewhat thinned, overlying epidermis with varying amounts of keratinization and within the dermis scattered nests and sheets of small, uniform, ovoid to round cells. These are not encapsulated and appear to be free within the dermal connective tissue. In the deeper layers the aggregates become more scant, although the nests always remain well defined. Noteworthy is the absence of change in the overlying epithelium. It is probable that these common lesions, as stated above, rarely if ever give rise to malignant melanomas and, as such, uncomplicated by other changes soon to be described, merit no surgical operation.

Junctional Nevus

This category includes the key to the development of malignancy. Clinically, juvenile nevi, unlike the former type, tend to be hairless, of varying shades of brown, and tend to be flat, not necessarily raised above the skin surface. Allen states that "the pigmented lesion on scrotum, palmar aspects of the hand and plantar surfaces of the feet may be assumed to be junctional nevi." Histologically the lesions differ markedly from the preceding group, presenting definite changes within the epidermis. Altered epidermal cells are found lying singly and in clusters, usually within the basal layers of the epidermis. These altered cells may either extend deeply within the dermis or project toward and through the surface of the epidermis to be desquamated. The altered epidermal cells assume the ability to form melanin and are said to have become neval cells. It is important to note that these changes frequently occur in discrete foci separated from one another, producing so-called skip areas of involvement. Thus, an entire lesion may apparently be included in a surgical specimen although a skip area has been totally missed. These dysplastic epidermal cells showing considerable cellular and nuclear variability form the basis of the origin of melanocarcinoma. It is

probably from these cells that melanocarcinoma develops. Hence it may be said that the junctional nevus is the basis from which malignant melanomas may arise. It is for this reason that nevi of the palms, soles and scrotum take on an especially ominous significance.

Compound Nevi

In approximately 12 per cent of the benign intradermal common moles of adults and 98 per cent of those of children there is an associated change in the overlying epidermis, so-called junctional change. Phrased differently, there is a combination of an intradermal nevus and a junctional nevus, together called a compound nevus. The association of these two types of nevi is more than coincidental and probably arises from the downward migration of clusters of cells from the epidermis into the dermis, producing the characteristic isolated clusters seen below the epidermis in the intradermal nevi. The intradermal nevus, when it is associated with a junctional nevus, is completely unaltered in its gross appearance. It is therefore quite impossible by clinical inspection alone to determine whether any given lesion is a pure intradermal nevus or is compounded with a junctional nevus. Moreover, as indicated above, the junctional component brings with it all the malignant potentiality of the pure junctional nevus. As mentioned above, approximately 98 per cent of intradermal moles in children show junctional changes, and only 12 per cent of these simple moles show such changes in adults. It is difficult to account for this decrease in incidence. Does this junctional component disappear from most lesions at puberty? The only conclusion that can be drawn is that the junctional change must regress in most of the intradermal nevi of adults. This disappearance of the potentially malignant element at puberty appears to dictate the need for the conservative handling of most nevi until after puberty. However, before this view can be accepted the next category of nevi must be considered.

Juvenile Melanoma

This term includes a subvariety of nevi occurring before puberty associated with junctional changes in the skin, *having the histologic appearance of malignant growths and behaving as benign lesions.* These differ from simple junctional nevi, which do not of necessity have the histologic appearance of cancer. The lesions are hairless, usually warty, pale red to brown, occurring anywhere on the body, commonly on the face. Histologically, they present great difficulty since they show marked variability in cell size, nuclear pattern, mitotic figures and multinucleated giant cells. Certainly, such a lesion on an adult would merit a diagnosis of melanocarcinoma. Yet, as shown by Spitz[25] and Pack,[26] they behave in general as benign lesions. In 13 cases only 1 death occurred. At puberty, however, these may take on the prognosis of the adult malignant melanoma. Obviously, there is some important correlation between the ability of these tumors to metastasize and take on autonomous invasive growth and puberty. Some endocrine role is strongly suggested. The inference to be drawn from the above anatomic data seems to be of great importance. Prior to puberty moles rarely become malignant clinically, even in the presence of a high incidence of junctional change.

Thus, it can be seen that Allen's reorientation of the problem of nevi permits a much more intelligent approach to their handling. The following points merit re-emphasis.

The common hairy mole, the intradermal nevus, rarely if ever gives rise to melanocarcinoma. It may, however, be associated with overlying junctional change in the epidermis.

Melanocarcinomas arise from junctional nevi. These moles are composed of intraepidermal cells that differentiate to become neval cells. These epidermal changes are quite atypical and form the antecedents of the malignant melanoma.

Virtually all nevi on the scrotum, palmar and plantar surfaces are junctional in type and hence are potentially malignant. This observation agrees with the occurrence of about one fifth of all melanocarcinomas at these sites.

Juvenile pre-puberal melanomas, while histologically appearing malignant, uncommonly behave so clinically. In the pre-puberal child they are rarely capable of invasive autonomous metastatic growth. With the advent of puberty the associated junctional changes that persist take on the prognosis of adult malignant melanomas and may be considered to be the precursors of melanocarcinoma.

Blue Nevus

This form of mole is usually readily recognizable grossly by its color. The dark-brown to slate-gray, deeply pigmented, hairless mole occurring on the dorsum of the hands or feet, or on the face, is probably of this variety. Histologically, these lesions occur intradermally and are usually composed of tight, whorled bundles of spindle cells. The individual cells tend to contain a large amount of melanin pigment. This tendency for the cell to be spindled is largely responsible for the earlier erroneous conception that these tumors were melanosarcomas. Indeed, all nevi are to begin with epithelial in origin, and moreover this type of blue nevus is rarely malignant. The overlying epidermis, as one might guess, uncommonly shows any junctional change. For some obscure reason, the intense pigmentation of these moles commonly excites clinical anxiety over the possibility of malignant degeneration. It is therefore perhaps well to

emphasize the benignity of the blue nevus and moreover to recall that pigmentation in general bears no relation to the malignancy of a mole. Some of the most potentially dangerous nevi are nonpigmented, and some of the most malignant invasive melanocarcinomas are amelanotic.

Shock

Knowledge of the pathology of shock has failed to keep pace with the clinical advances made in this entity. Most of the literature on this subject has been devoted entirely to considerations of the etiology, pathogenesis and treatment of this syndrome. The epochal observation of Bywaters et al.[27] on crush injuries seen during the bombing of London reawakened interest in the tissue changes accompanying such injury. As might have been anticipated from scattered clinical observations, many organs are described as being involved, specifically the heart, liver, adrenal glands and kidneys. The alterations in these four organs have features in common. The changes to be described all appear approximately eighteen hours after the shock-producing injury and become progressively more severe up to ninety-six hours, when they begin to decline with the onset of convalescence. Within the heart, liver and kidneys the appearance of intracellular fat vacuoles forms the dominant change. The adrenal glands, on the other hand, show a depletion of stainable lipid.

In somewhat more detail, approximately eighteen hours after the shocking injury, minute fat vacuoles appear within the myocardial fibers. This change appears to involve either the individual cell entirely or not at all. Thus, the lesion is quite focal and patchy, affecting certain cells within the myocardium and sparing immediately contiguous elements. With the longer survival periods the incidence and degree of fatty vacuolation drop sharply. It may be asked if the presence of this fat has any clinical significance. Bywaters, in his early descriptions of patients in shock, called attention to cardiac irregularities. He attributed these arrythmias to disturbances in the potassium blood levels of these patients. It is interesting to speculate whether the fat also played some role in this change. Shedding possible light on this point, a certain small number of patients autopsied at the Mallory Institute of Pathology, who died in what was termed cardiac failure with peripheral vascular collapse, have shown changes in the myocardium apparently quite similar to those described by Mallory.[28] None of these patients had antecedent shock, and although the etiology of this fatty degeneration was obscure, the time relations were such as to suggest that the fatty changes seen in the myocardium were important in the production of the final fatal issue. It is possible, therefore, that the myocardial changes described in shock contribute to the clinical picture as it is presently known.

The liver, too, is described as a site of pathology. At approximately the same interval, eighteen hours after the shock injury, minute intracellular fat droplets appear within the hepatic cells. These droplets are largely centrolobular in distribution and resemble what is termed fatty degeneration of liver cells — that is, the vacuoles are small and not coalescent and do not push the nucleus aside. In the more severe cases these fatty changes spread to involve the entire lobule. Necrosis of liver cells was not seen. In general, these changes resemble those found in the liver damage produced by such agents as phosphorus, chloroform and other forms of hepatotoxins. After the four-day period the severity of these histologic changes decreases. It must be assumed that they are reversible.

The relation of the adrenal gland to the shock state is by now well known. The changes found in the Mallory study conform well to those demonstrated in animal experiments. In pure shock uncomplicated by the concomitant presence of bacterial or toxic states, beginning after the eighteen-hour period, depletion of cortical lipids occurs. These changes affect the zona fasciculata of the adrenal cortex most markedly — that is, the middle third of the cortex. The two types of lipid present, the isotropic and the anisotropic elements, are both affected, the latter first. Necrosis of individual cortical cells occurs and creates small defects in the closely packed cells, producing what is called tubule or lumen formation. From animal studies and certain clinical reports it can be stated that these changes are probably reversible and are certainly compatible with continued survival. It should be noted that medullary changes are notably absent in pure shock. No clinical proof has yet been offered that depletion of this lipid creates a clinical deficiency of adrenal function contributing to the shock state.

Perhaps the most severely affected organ in shock is the kidney. The post-shock impairment of renal function, occasionally leading to anuria and death, is now well known. The outstanding microscopical features of these kidneys is the appearance of granular hemoglobin pigment casts in the tubules. In the tubules with these casts the underlying epithelium may be necrotic and destroyed. The surrounding interstitial tissue may show edema and a cellular infiltrate of lymphocytes, polymorphonuclear leukocytes and occasional plasma cells. The ascending limb of Henle's loop and distal convoluted tubules may also be affected. These may show fatty degeneration of the lining epithelium. Hyaline casts are occasionally found in these tubules, frequently associated with severe necrosis of the underlying tubular epithelium, to the point where the casts may erode their way into the interstitial tissue and produce focal granulo-

matous reactions. The over-all pattern of involvement of the kidneys varies from small focal areas of tubular damage with uninvolved intervening areas to widespread involvement of practically all the tubules. With survival of the patient beyond the post-shock period of three or four days, regeneration of the damaged epithelium begins and may continue to total repair of the injury.[29] It is not uncommon to find, at some later date, essentially normal kidneys in patients who have suffered post-shock azotemia and probable lower-nephron nephrosis. It is entirely possible that virtually perfect regeneration has restored the kidney to its former state. The clinical significances of these renal changes are too well known to need discussion.

To date the above lesions constitute the observed histologic sequelae of shock.

In conclusion, it should be re-emphasized that as yet the pathogenesis of these anatomic changes is still obscure. Although shock is almost certainly one of the most important factors, it may not be the sole cause. Any one of the various changes described may be seen in conditions other than shock. Thus, individually, these tissue changes are not specific. However, in the aggregate they very probably constitute a diagnostic anatomic picture.

References

1. Baxter, J. H., and Ashworth, C. T. Renal lesions in portal cirrhosis. *Arch. Path.* **41**:476-488, 1946.
2. Farquhar, J. D. Renal studies in acute infectious hepatitis. *Am. J. M. Sc.* **218**:291-297, 1949.
3. Kulka, P., Pearson, C. M., and Robbins, S. L. Destructive vacuolar nephropathy associated with intestinal disease. *Am. J. Path.* (in press).
4. Thomsen, S., and Vimtrup, B. Six fatal cases of infectious mononucleosis complicated by central respiratory paralysis. *Nord. med.* (*Hospitalstid.*) **4**:3295-3299, 1939.
5. Kilham, L., and Steigman, A. J. Infectious mononucleosis. *Lancet* **2**: 452-454, 1942.
6. Bang, J., and Wanscher, O. Histopathology of liver in infectious mononucleosis complicated by jaundice, investigated by aspiration biopsy. *Acta med. Scandinav.* **120**:437-446, 1945.
7. Custer, R. P., and Smith, E. B. Pathology of infectious mononucleosis. *Blood* **3**:830-857, 1948.
8. Peterson, R. E. Hepatic dysfunction in infectious mononucleosis; with review of literature. *J. Lab. & Clin. Med.* **33**:1258-1270, 1948.
9. Kass, E. H., and Robbins, S. L. Unpublished data.
10. Robbins, G. Personal communication.
11. Frazell, E. L., and Foote, F. W., Jr. Natural history of thyroid cancer: review of 301 cases. *J. Clin. Endocrinol.* **9**:1023-1030, 1949.
12. King, W. L. M., and Pemberton, J. So-called lateral aberrant thyroid tumors. *Surg., Gynec. & Obst.* **74**:991-1001, 1942.
13. Crile, G., Jr. Papillary carcinoma of thyroid and lateral cervical region: so-called "lateral aberrant thyroid." *Surg., Gynec. & Obst.* **85**:757-766, 1947.
14. Warren, S., and Feldman, J. D. Nature of lateral "aberrant" thyroid tumors. *Surg., Gynec. & Obst.* **88**:31-44, 1949.
15. Wozencraft, P., Foote, F. W., Jr., and Frazell, E. L. Occult carcinomas of thyroid: their bearing on concept of lateral aberrant thyroid tissue. *Cancer* **1**:574-583, 1948.
16. Gruber, W. Über die Glandula thyreoidea acessoria. *Virchows Arch. f. path. Anat.* **66**:447-454, 1876.
17. TeLinde, R. W. Intraepithelial carcinoma (in situ) of cervix uteri. *Surg., Gynec. & Obst.* **88**:792-794, 1949.
18. Galvin, G. A., and TeLinde, R. W. Present-day status of noninvasive cervical carcinomas. *Am. J. Obst. & Gynec.* **57**:15-36, 1949.
19. Foote, F. W., Jr., and Stewart, F. W. Anatomical distribution of intraepithelial epidermoid carcinoma of cervix. *Cancer* **1**:431-440, 1948.
20. Younge, P. A., Hertig, A. T., and Armstrong, D. Study of 135 cases of carcinoma in situ of cervix at Free Hospital for Women. *Am. J. Obst. & Gynec.* **58**:867-895, 1949.
21. TeLinde, R. W., and Galvin, G. A. Minimal histological changes in biopsies to justify diagnosis of cervical cancer. *Am. J. Obst. & Gynec.* **48**:774-797, 1944.
22. Meigs, J. V. *Tumors of the Female Pelvic Organs.* 533 pp. New York: Macmillan Co., 1934.
23. Allen, A. C. Reorientation on histogenesis and clinical significance of cutaneous nevi and melanomas. *Cancer* **2**:28-56, 1949.
24. Masson, P. Les naevi pigmentaires, tumeurs nerveuses. *Ann. d'anat. path.* **3**:417-453 and 657-696, 1926.
25. Spitz, S. Melanomas of childhood. *Am. J. Path.* **24**:591-610, 1948.
26. Pack, G. T. Clinical study of pigmented nevi and melanomas. Biology of melanomas. *Spec. Pub., New York Acad. Sc.* **4**:52-76, 1948.
27. Bywaters, E. G. L., and Dible, J. H. Renal lesions in traumatic anuria. *J. Path. & Bact.* **54**:111-120, 1942.
28. Mallory, T. B. Systemic pathology consequent to traumatic shock. *J. Mt. Sinai Hosp.* **16**:137-148, 1949.
29. Lucké, B. Lower nephron nephrosis (renal lesions of crush syndrome, of burns, transfusions, and other conditions affecting lower segments of nephrons). *Mil. Surgeon* **99**:371-396, 1946.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 36161

PRESENTATION OF CASE

A fifty-two-year-old steamship agent was admitted to the hospital because of precordial aches.

The patient stated that he was never strong but was always a nervous, hard worker with frequent need of rest. At twenty-three and twenty-four years of age he was forced to rest several months, on each occasion because of exhaustion. For many years he had easy fatigability and occasional slight dyspnea on exertion. Nine years before admission an x-ray examination of the chest revealed a round mass "in the region of the left pulmonary artery," which was said to have increased gradually in size.

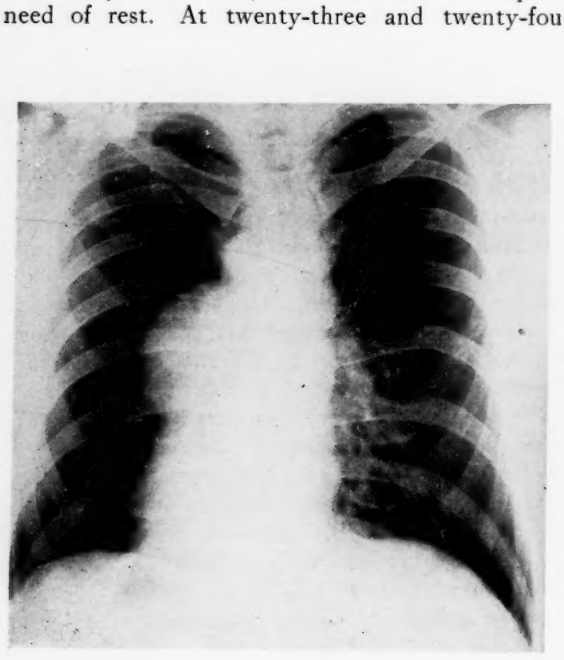

FIGURE 1.

For the past two years he again rested a great deal because of utter exhaustion from overwork. One year before admission, in addition to his easy fatigability, he developed sighing dyspnea and forceful intermittent palpitations. He also had had a precordial right-sided ache, with sharp brief stabs that at times lasted for hours. This aching pain was not related to meals or exertion and sometimes radiated to the neck but not to the arm or shoulder. He also complained of frontal headaches and occasional heavy midepigastric discomfort with exertion. At the age of fifteen he was discovered to have a complete situs inversus with dextrocardia.

Physical examination showed a well developed and well nourished man in no discomfort. Examination confirmed the presence of dextrocardia, but there were no evidences of cardiac abnormalities. The heart sounds were of good quality; there were no murmurs. The remainder of the physical examination was not remarkable.

The temperature was 98°F.; the pulse was 84 and regular, and the respirations 20. The blood pressure was 135 systolic, 80 diastolic.

Urinalysis revealed no abnormalities. The white-cell count was 10,800, with 63 per cent neutrophils, 31 per cent lymphocytes, 4 per cent monocytes and 2 per cent basophils. The hemoglobin was 17.0 gm. per 100 cc. The total protein was 6.7 gm., and the nonprotein nitrogen 27 mg. per 100 cc., and the prothrombin time 15 seconds (normal, 15 seconds). A blood Hinton test was negative. Radiologic examination revealed a complete situs inversus (Fig. 1). The heart shadow was on the right side and within normal limits. The stomach bubble was also on the right, and the liver apparently on the left. The colon also appeared to be on the right. The lung fields revealed no evidence of localized disease. The aorta was tortuous. Lying in the region of the pulmonary artery was a rather sharply defined shadow, 7 cm. in length and 4 cm. in diameter. This shadow was ovoid in shape, of homogeneous density and smooth in contour except for a suggestion of lobulation in the left anterior oblique projection. Fluoroscopically, this mass showed pulsation, which appeared expansive in type. The mass decreased in size when the patient inspired deeply and held his breath (modified Valsalva maneuver). A later examination failed to confirm the definite pulsatile nature of the mass and the change in the size of the shadow on deep inspiration. An electrocardiogram was within normal limits except for the changes consistent with the presence of dextrocardia: it showed a normal rhythm at a rate of 80, with a PR interval equal to 0.16, and a low upright T wave in Lead 1, upright T waves and small Q waves in Leads 2 and 3, low diphasic T wave in Lead AVL and upright T wave with small Q wave in Lead AVF. The T waves were upright in Leads V_1, V_2, V_3, V_4, V_5 and V_6.

On the first hospital day while being prepared for angiocardiography, the patient collapsed following infiltration of the right antecubital space with 1 per cent procaine. The pulse and blood pressure became unobtainable, and the patient was promptly given epinephrine and oxygen. He continued to be pale, weak and sweaty for over thirty minutes, with a blood pressure of 70 systolic, 50 diastolic, and a pulse of 80. On the following day he had completely recovered from this episode. A few days later an exploratory thoracotomy was performed.

Differential Diagnosis

Dr. F. Dennette Adams*: The first problem is whether or not a relation existed between the early symptoms described in the history and the lesion later found in the thorax. This is the type of case in which the discusser is at a decided disadvantage because of lack of opportunity personally to talk to the patient. No short record can bring out, as well as one would like, the nature of the patient's personality pattern. One could postulate that this man had some long-standing disease that produced weakness through the years. On the other hand, one could just as readily suppose that the history is that of an emotionally unstable person. Whereupon, most of the symptoms, especially those of his earlier years, could be regarded as having no relation to the intrathoracic lesion. When one reads that since youth the patient was never strong, and was always nervous, a hard worker, easily exhausted and in need of frequent rest, one is justified in doubting that these symptoms could be related to a lesion first discovered at the age of forty-three. At twenty-three and again at twenty-four, he was forced to rest several months because of exhaustion. This history could easily be that of an insecure, frustrated person who had the feeling that he was being imposed upon, that he had the worst job in the office and that everybody unloaded work on him. The easy fatigability and need for frequent rest could then be regarded as his means of escaping from a situation that at times became intolerable. In my experience the person who actually becomes weak or tired from routine work does not stay away from his job for three or four months at a time. He may require longer hours of sleep, short vacations or, if he is in the favorable income bracket, a week or so in Florida from time to time. But periods of utter exhaustion, each lasting three or four months, seem to be much more likely the result of emotional than physical difficulties and even suggest mild depression. All too frequently, one encounters patients of this category in private practice. Perhaps because I am so conditioned to them, it is difficult for me to attribute this man's exhaustion to any structural or metabolic disturbance, especially because of its periodicity. The sighing respiration bespeaks emotional rather than structural disease. The intermittent palpitations were most likely premature beats and of no importance in the current problem. The precordial ache with brief stabs could have been due either to premature beats or to neurocirculatory asthenia, not to structural heart disease. The aching pain radiating to the neck could have been referred from the lesion, which x-ray examination showed to be in the thorax. The frontal headaches may have been the earliest indication of venous congestion secondary to pressure within the thorax; the midepigastric discomfort on exertion, perhaps, was an early sign of mild congestion of the liver.

The physical examination provided no clues. I am interested in learning, Dr. Mallory, if this was a routine, perfunctory physical examination performed on a person in whom it was well established in advance that operation was to be carried out, or if some careful or inquisitive soul really searched for murmurs.

Dr. Tracy B. Mallory: He was examined by Dr. Paul D. White.

Dr. Adams: Who found no murmurs! I will accept that. I asked for this information because there are cardiovascular possibilities in this case. As we all know, some murmurs — for example, the diastolic blow of mild aortic regurgitation — are detectable only on meticulous auscultation.

Because of the length of time that the lesion is known to have existed, because during this period the patient remained in relatively good health and because the mass remained circumscribed and changed only to increase somewhat in size, a malignant neoplasm of the lung or mediastinum or any disease of mediastinal lymph nodes such as lymphoma, tuberculosis or metastatic cancer can be dismissed. So we can boil the problem down to that of a cardiovascular lesion or a benign mediastinal or pulmonary tumor. Before proceeding farther, I will ask Dr. Wyman to show us the x-ray films.

Dr. Stanley M. Wyman: The films of the chest show complete dextrocardia with the stomach bubble on the right side. There is a sharply defined homogenous density overlying the main pulmonary artery well seen in the oblique view and on a spot film (Fig. 1). The problem on x-ray examination was to decide whether that was the pulmonary artery or a mediastinal mass. There is a definite suggestion on this film and especially in the oblique view of a little lobulation of the soft-tissue density. The first time the patient was fluoroscoped, I felt that the mass changed on Valsalva experiment — that it became a little smaller. I also thought that the pulsations that I saw were expansile in character. I refluoroscoped the patient on the second day because I was not satisfied with that observation and this time was equally sure that the

*Physician, Massachusetts General Hospital.

mass did not change in size or shape with Valsalva experiment and that what pulsations I had seen had been transmitted from the underlying pulmonary artery. My conclusion was that the mass was probably not the pulmonary artery itself but a mediastinal mass overlying the pulmonary artery.

DR. ADAMS: In the anterior mediastinum?

DR. WYMAN: In the anterior mediastinum closely attached to the pulmonary artery.

DR. ADAMS: Now I am bogged down by the single laboratory report that might be of diagnostic significance: the hemoglobin of 17 gm. Dr. Mallory, was this checked or were any red-cell counts or other blood studies performed that might support that high figure?

DR. MALLORY: A second hemoglobin taken a very short time after the first was reported as 13.6 gm.

DR. ADAMS: If the high hemoglobin reading was substantiated, one would be forced to think in terms of some form of congenital heart disease in addition to the situs inversus. One might then postulate that the repeated periods of weakness were due to anoxia secondary to the congenital lesion. But I know of no congenital cardiovascular x-ray picture resembling that which Dr. Wyman has shown us. Furthermore, with the exception of pulmonary endarteritis, any such lesion, including pulmonary arteriovenous aneurysm, if sufficient to cause symptoms and a high hemoglobin should produce readily audible murmurs. So we must disregard the one high hemoglobin report and conclude that we have nothing to support a diagnosis of any congenital cardiovascular defect. Nor are there any facts to suggest aortic aneurysm. Dr. Wyman has indicated that the lesion did not pulsate or change in size during the respiratory cycle. There was no evidence of aortic valvulitis. Absence of disease of the aortic valve does not exclude aneurysm, but its presence would make one very suspicious of syphilis and hence of aneurysm. The negative blood Hinton test is further evidence against cardiovascular syphilis. One must therefore conclude that we are dealing with a benign anterior mediastinal tumor. The two most likely possibilities are dermoid cyst and thymoma. The relation between thymoma and myasthenia gravis is well established. Could this patient's weakness and fatigability through the years have been a variant of myasthenia gravis and attributable to the tumor? Here the history is all important. If I could be certain that the exhaustion and fatigue had been actually on a muscular or physical basis, I would make a diagnosis of thymoma. But as I interpret the history, the fatigue episodes seem more likely to have been on an emotional basis. Because of this I do not quite dare to attribute them to a structural or metabolic disturbance. If more details of these attacks and of the exhaustion were available, I could readily change my mind. So I am going to guess chiefly on the law of probability that the lesion was a congenital dermoid cyst. It was probably benign but could show areas of recent malignant change.

CLINICAL DIAGNOSES

Mediastinal tumor.
Situs inversus.

DR. ADAMS'S DIAGNOSIS

Mediastinal tumor; probable dermoid cyst.

ANATOMICAL DIAGNOSIS

Thymoma.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient's thorax was explored by Dr. Richard H. Sweet, who found a tumor overlying the heart and great vessels obviously arising in the anterior mediastinum. It was lobulated and nestled very closely in among the great vessels, but he was able to get it out, he believed, intact. The specimen as we received it weighed about 150 gm., was definitely lobulated and was a solid tumor. Microscopical examination showed an appearance that puzzled us for some time. There were portions of tumor that were reasonably characteristic of thymoma, consisting of large masses or sheets of epithelial cells mixed with moderate numbers of lymphocytes. There were also, however, some areas that looked fibrous and spindle shaped and almost suggested a neurofibroma. Dr. Castleman, who has been studying these tumors of the thymus, eventually decided that it was all consistent with a diagnosis of thymoma, and in certain thymic tumors we have seen, these spindle-cell areas were suggested or even frankly developed. Apparently, the epithelial reticulum of the thymus can on occasion simulate connective tissue very closely. Since this man had a thymoma it is quite within the limits of possibility that he had a mild myasthenia. No therapeutic test with Prostigmine was ever made.

ADDENDUM

DR. ADAMS: My interest in the possible relation between the early symptoms and the tumor prompted me, on the day following the above discussion, to ask Dr. Paul D. White if he would communicate with the patient and find out the current status. Dr. White has kindly done so and sent me the following quotation from a letter received from the patient eight months after operation: "I have felt perfectly all right since the operation with no symptoms of weakness, fatigue or any other I had before." This seems to indicate that perhaps my interpretation of the fatigability and exhaustion in the patient's earlier years was incorrect and that there may have been a relation between these symptoms and the tumor.

CASE 36162

Presentation of Case

First admission. A fifty-four-year-old woman was admitted to the hospital for study because of abdominal distress.

Two years prior to admission a left radical mastectomy was performed at another hospital, and a pathological diagnosis of carcinoma of the breast with uninvolved axillary lymph nodes was made. Four months before admission she was bothered by "sinus" trouble, following which she had eight attacks of upper abdominal distress with nausea and vomiting recurring at intervals. Vague substernal burning accompanied some of these attacks. Other complaints at this admission were indigestion, gaseous eructation and the passage of flatus several hours after meals. Except for a few loose bowel movements two days before admission the bowel habits had always been regular. There was no history of definite pain or of jaundice.

She had been afflicted with an occasional attack of "sinus" trouble and an occasional attack of hives in the past. The menopause had occurred five years before admission.

Physical examination revealed a well developed, well nourished woman in no acute distress. There was a well healed, left radical mastectomy scar with no evidence of local recurrence of tumor and a left inguinal herniorrhaphy scar. Examination of the heart and lungs was negative. The abdomen was soft; there was no tenderness or spasm, and no masses or organs were palpable.

The temperature was 98.2°F., the pulse 84, and the respirations 20. The blood pressure was 150 systolic, 85 diastolic.

Examination of the blood disclosed a white-cell count of 6400 and a hemoglobin of 15.5 gm. An x-ray film of the chest was normal. A Graham test showed a well filled gall bladder and no shadows suggestive of stones. After a fatty meal the gall bladder contracted slightly, revealing no evidence of intrinsic disease. A barium enema showed several diverticula in the midsigmoid, with some spasm and with prominence of the mucosa in the sigmoid. There was no evidence of obstruction in the large bowel; the barium flowed readily through the colon to fill the cecum. All visualized bones appeared diffusely osteoporotic. A gastrointestinal series was negative except for a large hiatus hernia, measuring 6.0 cm. in diameter, which emptied readily. The spleen appeared larger than normal.

The patient was discharged on the second hospital day.

Second admission (four months later). Since the last admission the patient had experienced pain in the upper abdomen, belt-like in distribution and extending bilaterally to the lumbar region. The pain was prolonged, steady and somewhat more severe on the right side. For the three weeks previous to this admission the patient had an acute sore throat, which was treated with penicillin. During this period her appetite had declined, and there were episodes of vomiting. It was reported that two days before admission she had lost 2500 cc. of fluid by this route. Just prior to this admission some change had occurred in her symptomatology and she received two 20-mg. doses of Pantopon.

Physical examination revealed a drowsy, confused woman, who appeared chronically ill. The pupils were constricted. The pharynx was injected and had a few spots of white exudate. The abdomen was tender bilaterally, more marked on the right. Palpation was difficult because of the patient's condition, but it was believed that there was a mass in the epigastrium. This could not be definitely defined as to origin or size. The liver was not enlarged to percussion. The spleen and kidneys were not palpable. The abdomen was tympanitic, and evidence of peristalsis was heard. There was no costovertebral-angle tenderness.

The temperature was 98°F., the pulse 80, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

The white-cell count was 19,000, and the hemoglobin 11.6 gm. The urine gave a + test for albumin and an orange sugar reaction, and the sediment contained 10 white blood cells per high-power field. The specific gravity was 1.018, and a test for acetone was negative. The nonprotein nitrogen was 22 mg., the total protein 6.1 gm., and the fasting blood sugar 99 mg. per 100 cc., the chloride 95 milliequiv. per liter, and the prothrombin time 17 seconds (control, 15 seconds). Three stool examinations were guaiac negative, and one was negative for amebas. A blood Hinton test was negative.

A chest film showed the right leaf of the diaphragm to lie considerably higher than previously. There were several strand-like areas of density in both lower-lung fields, more on the right than the left, consistent with atelectasis. A plain film of the abdomen showed the liver shadow to be apparently larger than at the first admission. No definite abnormal soft-tissue shadows or localized bone destruction was seen.

The patient was treated with intravenous injection of glucose, liquids by mouth, sedatives, hypnotics and warm gargles. On the day following admission the temperature rose to 100.6°F., and the pulse to 98. In each of the subsequent four days the temperature rose in the late afternoon to 99.5°F. At other times in the day it was normal. She had diarrhea (eight to ten loose movements per day), which continued during her stay. Abdominal examination confirmed the finding of a mass in the epigastrium, somewhat over toward the right. It was believed that this did not represent the liver. This area was consistently tender and so examination was difficult. Subjectively, the complaints were

somewhat vague, and the patient kept saying that she wished to be operated upon "and fixed up inside." One observer believed that if organic disease was present it coexisted with a personality neurosis.

The white-cell count on the third and fifth hospital days were 13,500 and 7,900 respectively. Urinalysis on the fifth hospital day was normal.

A gastrointestinal series showed that the duodenal cap and proximal portion of the second part of the duodenum were displaced forward, and there appeared to be extrinsic compression of the distal portion of the cap. The liver appeared to be definitely larger than previously. At the end of six hours considerable barium remained in the stomach; the remainder was in loops of small bowel and in the right colon. The palpable abdominal mass appeared to lie just below the antrum of the stomach. A barium enema done on the sixth hospital day showed the transverse colon to be displaced downward to a considerable degree, being separated from the stomach by a distance of 11 cm. The antrum of the stomach was displaced upward in the midline. Barium flowed readily through the colon to fill the cecum. There was no definite evidence of intrinsic disease in the colon or of involvement by the mass, which was regarded as probably lying in the omentum, or possibly in the mesentery between the stomach and transverse colon.

An operation was performed on the seventh hospital day.

Differential Diagnosis

Dr. Marshall K. Bartlett*: May we see the x-ray films now?

Dr. Stanley M. Wyman: The x-ray films from the original examination show no definite intrinsic disease in the chest. One film of the gall-bladder examination is not remarkable. The colon appears intrinsically normal, and the stomach is not remarkable except for this large hiatus hernia. The second examination shows quite pronounced changes. Although the patient was lying down, the right leaf of the diaphragm appears to have risen considerably, and there is apparently atelectasis in both lower-lung fields. The liver shadow extends both lower and higher than previously, which is consistent with liver enlargement. The most striking finding is separation of the stomach in its distal portion from the midtransverse colon, which had previously lain in normal relation. A definite mass could be palpated in this region. It was tender and seemed to move somewhat. There was no intrinsic involvement of the stomach or colon. The duodenum appears also to be displaced anteriorly and perhaps laterally somewhat, suggesting pressure from the pancreas.

Dr. Bartlett: Do we know whether the right leaf of the diaphragm moved with respirations or not?

Dr. Wyman: I think it did move.

*Associate visiting surgeon, Massachusetts General Hospital.

Dr. Bartlett: We have the problem of a fifty-four-year-old woman whose first admission was caused by a series of attacks of upper abdominal distress, eight in number, which I judge from the record were not particularly severe. She was sent home after only two days in the hospital and then returned four months later. During this interval between admissions the patient developed for the first time pain localized in the epigastrium and upper abdomen, anorexia and considerable vomiting. On physical examination at the second admission a new finding was a mass in the epigastrium.

What was the nature of this mass? The things we know about it are that it was of relatively short duration; at least if it was present at the time of the first admission, it was not large enough to be demonstrable. It had become so in the interval. The mass was located in the epigastrium perhaps more to the right and displaced various organs. It also displaced the antrum of the stomach upward, and the duodenum anteriorly, and apparently displaced the transverse colon downward. The mass was tender and the patient had had pain, which we assume was related to it. What kind of a mass would fit these requirements? Is it possible that this was all related to the carcinoma of the breast two years before entry? The liver had become enlarged. Metastatic carcinoma from the breast to the liver occurs, but it is not too common. It might explain the liver enlargement, but could it explain the mass in the epigastrium? We would have to postulate some rather devious lymphatic channels. We know that there are direct lymphatic channels that go from the breast to the diaphragm, but to get from the diaphragm down to the epigastrium I think we would have to assume retrogression in the lymphatic channels, which I do not think is very likely. The first barium-enema examination of the colon suggested some minimal changes, but these were not confirmed at the second, so that it seems highly unlikely that a lesion in the colon produced a secondary mass in the epigastrium. The possibility of amebic abscess comes to mind, but it is very rare and I should think that the x-ray films of the colon would have been more helpful in such a situation. Could it have been echinococcal disease with an abdominal mass and involvement of the liver? We are not told where this woman had lived or what her nationality was, but I think that disease is an outside chance.

What kind of primary mass could she have had? Was this something that arose in the stomach or duodenum? I think the evidence is that it was extrinsic to the stomach and duodenum. A lesion of the gall bladder seems to be a fairly remote possibility. The gall bladder was normal by x-ray examination, and certainly no lesion of the gall bladder should displace the various organs as they were affected here. To implicate the kidney I think we should have to assume that there was a horseshoe kidney extending across the midline, and this should

have been present on physical examination. Could it have been something arising in the omentum between the stomach and the colon? I think the type of pain she had was against that. Band-like pain radiating around to the lumbar region suggests to me some structure that is quite intimately related to the posterior abdominal wall if not actually retroperitoneal. The organ that I have left until last and that seems best to fit the situation is the pancreas. From its position I think it could have caused the various phenomena that were present here. Certainly, a mass in the pancreas could displace the duodenum anteriorly, and if it became large enough I think it could displace the antrum and the transverse colon.

And now to attack the mass in a different way, was it inflammatory or neoplastic? It had become large enough to be recognized in a period of four months. A neoplasm could progress that rapidly, and an inflammatory mass probably could also. The intermittent symptoms in the early phase are suggestive of recurrent inflammatory disease rather than neoplasm. The tenderness seems to favor the inflammatory process, as does the low-grade temperature and elevated white-cell count. The anorexia and vomiting do not help me much one way or the other. They could go with either type of process. The enlargement of the liver is hard for me to account for on the basis of an inflammatory process. It would be more consistent with metastases to the liver. However, it seems to me that the best explanation for this is recurrent inflammatory disease in the pancreas. The eight attacks the patient had prior to the first admission could well have been mild bouts of pancreatitis. I think the process had gone on and that she had developed a mass in the pancreas, which I am going to assume was on an inflammatory basis although I see no way of ruling out an underlying malignant process. A retroperitoneal cancer arising in the region of the pancreas but not from the pancreas also is a possibility that I have no way of ruling out, but I think the most likely diagnosis is inflammatory disease of the pancreas.

Clinical Diagnosis

Pancreatic cyst?

Dr. Bartlett's Diagnosis

Pancreatitis, recurrent.

Anatomical Diagnosis

Pancreatitis, hemorrhagic, with fat necrosis.

Pathological Discussion

Dr. Tracy B. Mallory: This patient was operated on by Dr. Leland S. McKittrick, who found as soon as he entered the abdomen that all peritoneal surfaces were flecked with fat necrosis. This was confirmed by biopsy. On exploring further, he found a very large hemorrhagic and necrotic mass in the mesentery lying between the stomach and colon, and this appeared to be the mass that had been palpated. It was surrounded on every side by foci of fat necrosis. The pancreas itself was also greatly enlarged and showed extensive hemorrhagic necrosis. He thought from the appearance at operation that the process was subsiding. It was not technically possible to drain the common duct, and he decided to do nothing. The patient has made a reasonably satisfactory convalescence.

Dr. Allen G. Brailey: What about the liver?

Dr. Mallory: It seemed quite normal at operation.

Dr. Bartlett: I should like to ask how often neoplasm of the pancreas will produce bouts of pancreatitis. I do not think I have ever seen it. The surgeon sees chronic pancreatitis associated with neoplasm of the pancreas at operation, but I do not think that it can be recognized clinically as pancreatitis.

Dr. Mallory: I do not remember ever seeing it either.

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COMPULSORY OR VOLUNTARY?

The *Journal* this week contains statements by two well known exponents of the opposing views on compulsory and voluntary health insurance, the words "health insurance" in the present controversy being generally accepted as referring to various plans devised to meet the costs of personal medical attention.

These approaches to the problem of better medical care might be called the quick and the cautious; with no reflection on either philosophy they could be considered as representing the cutting of the Gordian knot on the one hand, believed by many to be a destructive act, and a continued effort at untying it on the other.

Each of these opposing plans has the same basic objectives — the delivery to the greatest possible number of persons of the best possible medical care on the most economical terms. The principles involved are better understood if the term "socialized medicine" is abandoned. It has been too broadly interpreted to let it be any longer definitively useful.

The proponents of compulsory insurance as represented by Dr. Frothingham believe that the elimination of the "dollar barrier" between patient and physician would also eliminate the dangerous procedures of self-medication and drug-clerk diagnosis and permit an unrestricted but restrained employment of the physician's services by everyone.

They believe that lay control in the development of the rules to govern medical practice will guarantee the quality of the care delivered, and that lay trustees of hospitals have already developed better regulations for the delivery of this service than has organized medicine.

It is moreover their conviction, so far as can be determined, that a plan of compulsory insurance as proposed would come to a full stop at its optimum level of desirability without setting up a chain reaction that would end in the complete dominance of medical practice by the state.

The important arguments of the opponents of compulsory insurance, as presented by Dr. McKittrick, are equally simple. A Government bureau, according to this presentation, cannot replace private responsibility, and he envisages the first step in Government control as leading on to complete bureaucracy.

Without the stimulus of private enterprise, he believes, the quality of medical care will deteriorate even as its quantity may increase. Moreover, as the Report of the Hoover Commission indicates, costs under Government control are almost certain to be excessive.

On these bases the people of the country are even now making the decision, to be announced through their representatives, by what method they will receive and pay for their medical care in the foreseeable future, and of what quality that care will be.

NORFOLK DISTRICT CENTENNIAL

The Norfolk District Medical Society, nothing if not alert, appears to have taken the ball away from its somewhat older metropolitan sibling,

Suffolk, in the matter of centennial observances. Suffolk, a forty-niner so far as centenarianism is concerned, last year let the occasion pass unobserved, not unwittingly but perhaps bored with its own antiquity.

Age, however, is relative, and Norfolk and Suffolk, unless false starts should be counted, are merely on the cradle roll of the organized districts of the Massachusetts Medical Society. The Boston District Society, authorized in 1803, made its real start in 1809 and held meetings until 1813, then went underground, emerging with the establishment of the Suffolk District in 1849.

Norfolk petitioned the Council for establishment in 1806, but nothing happened until 1850. Already, in 1804, Essex Southern and Worcester had been founded; Berkshire, after its own false start in 1807, had a charter accepted in 1820; Hampshire was established in 1831, Bristol South in 1839, and Barnstable and Hampden in 1840; Essex North appeared in 1841, Middlesex North in 1844, and Bristol North, in company with Suffolk, in 1849. The big year, 1850, produced not only Norfolk but Middlesex East, Middlesex South and Plymouth; Franklin, in 1851, Worcester North, in 1858, and Norfolk South, in 1884, completed the present list of eighteen district societies.

Norfolk, like the infant in the story once current, was the twin that "did something." Not only has the Society embarked on an admirable hundredth anniversary educational program, but it is about to highlight its centenary with an anniversary dinner on May 3, at which President Henry M. Wriston, of Brown University, will be the speaker of the evening, and many other prominent guests will be present.

TUBERCULOSIS — STILL A PROBLEM

Governor Paul A. Dever, in his annual address to the Massachusetts Legislature, referred to the approaching completion of the tuberculosis survey in Metropolitan Boston, which resulted in the x-ray examination of more than 500,000 persons. Such an outstanding response by the public was due in part to the excellent publicity and careful planning given this project and also to the valuable assistance of many volunteer workers.

Governor Dever pointed out that the results of the Boston survey have emphasized the necessity for setting up tuberculosis clinics operated by the Department of Public Health to provide more adequate finding of early cases. The Massachusetts Department of Public Health sanatoriums at Westfield, Rutland, Lakeville and North Reading are now operating 14 diagnostic clinics, and 17 additional clinics are operated by county sanatoriums in Middlesex, Essex, Plymouth, Norfolk and Hampshire Counties. These clinics are essentially diagnostic and are used primarily for the examination of contacts of known or suspected cases referred by family physicians. Each city with a population of over 50,000 is required by law to provide diagnostic facilities for the finding of tuberculosis.

The necessity for mass x-ray study of the population is demonstrated by the fact that only a fourth of all new cases are traceable to known cases of tuberculosis. This finding indicates the existence of a large unrecognized reservoir of bacilli, which is a possible source of infection to many susceptible persons. Only by the extension of case finding by mass x-ray examinations of large population groups can people suffering from incipient tuberculosis be assured of a reasonable chance for arresting the disease and returning to their homes as self-sustaining, independent citizens. These community surveys, such as the one just completed in Metropolitan Boston, are especially important in that they reveal cases in this early, hopeful phase of the disease; 60 to 70 per cent are minimal, compared with a 10 to 15 per cent mimimal stage reported by other methods of case finding. The medical profession wishes to assure Governor Dever and the Department of Public Health of its support in this case-finding program for early diagnosis of tuberculosis.

About 25 per cent of the cases with positive findings were "unsettled" cases and not the responsibility of any municipality. They are, as the Governor stated:

> Cases for which the Commonwealth must assume responsibility. Sufficient numbers of them require hospitalization so that the facilities of the metropolitan area have become overtaxed. We shall have to authorize expenditures at once to recondition some of the other state hospitals.

In addition, in a recent release to the press the Governor has indicated his interest in obtaining the Murphy General Hospital to replace the outdated Rutland Sanatorium. His Excellency is to be complimented upon this farsighted move, since it not only will save the Commonwealth millions of dollars but also will make possible the saving of lives by providing additional beds for the care of patients. This practical plan, which combines early case finding with adequate hospitalization in a modern structure, will do more to reduce the incidence of tuberculosis to a minimum than any other plan that the Commonwealth could adopt. It is sincerely hoped that the Department of Public Health will be granted the necessary appropriation to increase its case-finding program through mass surveys and that the Governor will succeed in obtaining the Murphy General Hospital for more adequate care of tuberculosis patients.

MISSOURI STATE MEDICAL ASSOCIATION

THE hundredth anniversary of the Missouri State Medical Association was celebrated at the Hotel Jefferson in St. Louis from March 26 to 29. Outstanding physicians throughout the country took part in the scientific program, which included carefully selected papers on a variety of subjects. A particularly welcome item was the history of the Association, written by Dr. Robert E. Schlueter, which was presented to those who attended the annual banquet in honor of past presidents. For the first time in St. Louis, actual operations, as well as special medical clinics, were portrayed over television.

The Association is to be congratulated not only on the occasion that marks the first hundred years of its existence but also on the quality and interest of the program, which commemorated the centennial appropriately and felicitously.

The report of the City Physician to the Boston Board of Aldermen, shows that he has vaccinated, during the last 3 months, 1630 persons. One paper states it to be 8638 — a number almost incredible, and without precedent. As the account is from a newspaper report of the doings of the city officers, it is presumed to be incorrect.

Boston M. & S. J., *April 17, 1850*

MASSACHUSETTS MEDICAL SOCIETY

SURVEY OF PHYSICIANS' INCOMES

The Bureau of Medical Economic Research of the American Medical Association has been authorized by the Board of Trustees to co-operate with the Office of Business Economics of the United States Department of Commerce in conducting a survey of physicians' incomes. The survey will start this spring, and an analysis of the results will be published by the Department of Commerce next fall in its publication "Survey of Current Business."

Physicians are assured that the survey has no relation to the Bureau of Internal Revenue and that this information could not have been obtained by the Department of Commerce from the Bureau.

Two questionnaire forms will be sent out: a short form requesting income data for 1949 only, and a long form covering the years 1945 through 1949. All are returned unsigned. The survey will cover an impartial selection of 125,000 of the 200,000 physicians of the country, a short form going to every other name in the file, and a long form to every fourth physician of the remaining 100,000.

It is believed that the national averages in some surveys have been too high because many physicians without bookkeeping secretaries will ignore such questionnaires. Consequently, the Bureau of Medical Economic Research urges all doctors, especially those with small practices, to fill out and return the questionnaires. Only by an accurate analysis of this nature can a reliable estimate be made of how much the American people are paying their physicians.

DEATH

WEISS — Bernard Weiss, M.D., of Mattapan, died on March 27. He was in his sixty-fourth year.

Dr. Weiss received his degree from Tufts College Medical School in 1916. He was a fellow of the American Medical Association.

His widow, a son and two daughters survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The May schedule for Consultation Clinics for Crippled Children in Massachusetts under the provisions of the Social Security Act follows:

Orthopedic Clinics	Date	Clinic Consultant
Salem	May 1	Paul W. Hugenberger
Haverhill	May 3	William T. Green
Greenfield	May 4	Charles L. Sturdevant
Lowell	May 5	Albert H. Brewster
Gardner	May 9	Carter R. Rowe
Brockton	May 11	George W. Van Gorder
Springfield	May 16	Garry deN. Hough, Jr.
Pittsfield	May 17	Frank A. Slowick
Worcester	May 19	John W. O'Meara
Fall River	May 22	David S. Grice
Hyannis	May 25	Paul L. Norton

Rheumatic Fever Clinics	Dates
Fitchburg	May 3, 10, 17, 24, 31
North Reading	May 2, 9, 16, 23

Plastic Clinics	Consultant
Eastern Massachusetts	Bradford Cannon
Clinics bi-monthly	
Western Massachusetts	Joseph M. Baker
Clinics monthly	

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

CORRESPONDENCE

RELATION OF SERUM CHOLESTEROL TO ARCUS SENILIS

To the Editor: In the article entitled "Arcus Senilis and Serum Cholesterol Levels in the Aleut," by Drs. Garn and Gertler, which appeared in the February 23 issue of the *Journal*, it is stated that "Recently, Boas et al. have devoted considerable attention to arcus senilis in relation to disorders of cholesterol metabolism, and they have demonstrated a higher incidence in persons with hypercholesterolemia. . . . They have assumed a causal relation between augmented serum cholesterol levels and arcus senilis, noting that this relation need not be invariable — that is, the correlation was not a perfect correlation."

The authors raise the objection that our material was "sorted" by the selection only of patients with hypercholesterolemia or with conditions commonly accompanied by hypercholesterolemia. In actual fact the first study, entitled "Arcus Senilis and Arteriosclerosis," (*J. Mt. Sinai Hosp.* **12**:79-83, 1945) represents a study of the incidence of the corneal arcus in 1000 consecutive office patients examined because of some cardiac complaint. Only half these had coronary-artery disease. It was pointed out that these patients were not a true sample of the general population. Cholesterol studies were not included.

In subsequent publications, entitled, respectively, "Familial Hypercholesterolemia (Xanthomatosis) and Atherosclerosis) (*J. Mt. Sinai Hosp.* **12**:84-86, 1945), "Hereditary Disturbance of Cholesterol Metabolism: Factor in genesis of atherosclerosis" (*Am. Heart J.* **35**:611-622, 1948) and "Genetics of Atherosclerosis" (*J. A. M. A.* **141**:246-254, 1949), the syndrome of hereditary hypercholesterolemia as related to coronary atherosclerosis was investigated. Corneal arcus was encountered as a common associated clinical finding in patients with coronary-artery disease under the age of fifty years. Among 122 such patients, corneal arcus was found in 22, of whom 17 had hypercholesterolemia (serum cholesterol of 300 mg. per 100 cc. or more). In another study of 201 persons with familial xanthomatosis, 35 were found to have arcus, of whom 28 had hypercholesterolemia.

It should be emphasized that these studies were not designed to investigate the relation of disturbed lipid metabolism to corneal arcus, but rather that between coronary atherosclerosis and hypercholesterolemia. Xanthelasma as well as corneal arcus was noted to occur frequently in our patients with hypercholesterolemia. However, this does not imply that either corneal arcus or xanthelasma *in the population at large* is related to high blood cholesterol levels, although such a possibility has often been discussed. Drs. Garn and Gertler should not have given the impression that the implication of our data is that "the disturbance of cholesterol metabolism must precede the appearance of arcus senilis and that a group of subjects selected on the basis of arcus senilis alone should show an elevated serum cholesterol level compared to others in the same group." We have made no such statement and are well aware that many patients with arcus have normal serum cholesterol.

Nonetheless, it is worthy of emphasis that given a young patient who exhibits corneal arcus and a history suggestive of coronary-artery disease, determination of serum cholesterol is indicated in the patient and in members of his family as well. In some persons the innocuous corneal arcus may be a clue to disturbed lipid metabolism.

Ernst P. Boas, M.D.
David Adlersberg, M.D.
Albert D. Parets, M.D.

New York City

ORIGIN OF SPLENIC CYST

To the Editor: In the March 16 issue of the *Journal* the case presented (Case 36112) perhaps warrants some additional comment.

The patient presented herself with a left-upper-quadrant mass, which ultimately proved to be a splenic cyst of traumatic origin. Although severe, generalized trauma had been sustained five months prior to admission, no symptoms referable to the spleen were present at that time. In a search for the origin of this cyst it is necessary to probe further into the past history of the patient.

One year prior to the present illness the patient had experienced a febrile illness with symptoms of fatigue, anorexia, headache and soreness of the neck. The physical findings consisted of slight cervical adenopathy and hepatomegaly. The blood smear showed atypical lymphocytes, monocytes and "blast" forms. Notwithstanding a negative heterophil-antibody test, it must be assumed that the patient had infectious mononucleosis. Blast forms are not uncommonly seen in the peripheral blood transiently in this benign condition. During the hospital stay the hemoglobin dropped precipitously over a six-day period; the spleen became palpable, and the patient icteric. In the protocol this episode is attributed to acute hemolysis. However, no mention is made of antibody studies, a Coombs test and so forth.

In the light of the finding of a traumatic splenic cyst one year later it seems most likely that the episode was due to subcapsular splenic hemorrhage (with or without rupture of the spleen) in a patient suffering from infectious mononucleosis. The high indirect bilirubin, the splenic mass and the acute fall in hemoglobin are compatible with loculated interabdominal hemorrhage.

This untoward complication in an otherwise benign disease has been reported most recently by Timmes, Averill and Metcalfe, in an article entitled "Splenic Rupture in Infectious Mononucleosis" (*New Eng. J. Med.* **239**:173-175, 1948), and by Brien, in a study on the subject "Infectious Mononucleosis — Complications" (*Canad. M. A. J.* **56**:499-502, 1947).

The serious consequences of such hemorrhage and rupture have led to an admonition against repeated palpation of the spleen as well as heavy exertion. The rapid development of an anemia in a patient presumably suffering from a virus disease should be suggestive of splenic hemorrhage, in addition to the usual considerations.

Martin Rosenthal, M.D.

New England Center Hospital
Boston

IN DEFENSE OF THE INDUSTRIAL PHYSICIAN

To the Editor: George Vash, M.D., in his letter in the March 23 issue of the *Journal*, makes several derogatory statements about industrial medicine to which I must reply.

In the first place, I cannot permit the following statement to go unchallenged:

> The real threat to honest medicine today looms in other quarters. Industry has its own doctors, and, more often than not, the company doctor creates distrust, dispenses free advice and free pills and thus causes the patients to lose confidence in the family doctor. . . .

In Massachusetts scores of industrial physicians are on a part-time basis. They are the very physicians who practice in the respective communities. Furthermore, the objective of industrial medical departments, as pertains to nonindustrial illness, is to give the patient the best possible advice, referring him for definitive diagnosis and treatment to his family physician. This procedure tends to reduce to a minimum the impediment to effective therapy present even in this day of miracle skills and drugs. I refer to the prolonged delay between symptomatology and treatment that exists in too many cases.

The industrial physician makes no pretense at taking the place of the private practitioner. They complement and work closely with one another, or they should. Maybe the basic difficulty in the two cases cited was a failure to cooperate with one another.

Certainly a profession that is the subject of much misunderstanding, and even criticism, should make every effort for complete understanding among its own members. Only in this way shall we attain our common objective of optimum health for all.

JOHN J. POUTAS, M.D.
Medical Director

Lever Brothers Company
New York 13, New York

CLOSING OF MURPHY GENERAL HOSPITAL

To the Editor: To those who are deeply concerned in providing proper medical care for the armed forces in New England, the proposed closing of Murphy General Hospital in Waltham, Massachusetts, has come as a severe blow.

Murphy General Hospital was built and equipped in 1944 at an expenditure of approximately $5,000,000. It is of brick construction throughout and has a life expectancy of more than thirty years. The fact that it is close to all the leading medical institutions of Boston has enabled young doctors to participate in ward rounds in Boston hospitals — a plan that has allowed them to acquire valuable experience in the past. Inasmuch as the trend in recent years has been to improve the professional standards in the Army Medical Corps, the present plan of abandoning Murphy General Hospital and reinvesting money in the temporary wooden structures at Fort Devens, which will eventually have to be abandoned, does not appear to be in the interests of the patients, the medical profession or the taxpayers. It will be extremely difficult for civilian consultants to make the long trip to Fort Devens.

It was learned recently in Washington that there will be a critical shortage of doctors this summer, as men returning from overseas as well as our own young doctors complete their tours of duty; therefore, it appears a serious blow to close this hospital. It had been planned to set up an intern training program at the hospital, and this consideration, together with the fact that medical reserve officers in this area would be tempted to return for a tour of duty because of the hospital's facilities and close proximity to Boston, seems an added reason for maintaining Murphy General Hospital.

The bed capacity authorized by the Secretary of Defense for Fort Devens is 200, which is believed inadequate since Murphy General Hospital has been caring for troops stationed throughout the New England area, sections of New York and New Jersey, as well as patients flown in from overseas via the surrounding air bases. Admiral Swanson testified at the Congressional hearing on April 4 at Murphy General Hospital, that Chelsea Naval Hospital is not in a position to handle the additional patient load that will result from the closing of Murphy General Hospital.

The tentative figure set by the Secretary of Defense for repairing buildings at Fort Devens is $691,000. It was brought out during the hearing that this would be a sheer waste of money, that the wooden hospital buildings at Fort Devens had been constructed in 1941 as a war-time emergency, that in that respect their mission had been accomplished but that further investment of public funds in these buildings is unwarranted, and that in the long run, it would be cheaper to replace rather than reconstruct. It was further brought out in the testimony that a serious fire hazard exists at Station Hospital, Fort Devens, to which bed-ridden patients should not be exposed.

Testimony was offered by well known professional men, civic leaders, representatives of veterans' organizations and hospital patients for the retention of the hospital in the interests of the armed forces. Dr. Vlado A. Getting, Massachusetts Commissioner of Public Health, said that the Commonwealth of Massachusetts would be glad to have the hospital "lock, stock and barrel" should the Army abandon it.

It is understood that Chairman L. Mendell Rivers (S.C.), Armed Service Sub-committee, is recommending retention of the hospital.

(MRS.) HELEN F. KELLEY
Secretary, Lodge 1190
American Federation of Government Employes

BOOK REVIEWS

Histopathology of the Skin. By Walter F. Lever, M.D. 8°, 449 pp., with 221 illustrations. Philadelphia: J. B. Lippincott Company, 1949. $10.00.

This book is very complete and includes the essentials necessary for the training of a dermatologist in dermatopathology; it is broad enough to be used as a reference book for the general pathologist. All dermatologists may not agree with some of the clinical definitions, nor pathologists with all the opinions on pathology; however, when necessary, conflicting opinions and an extensive bibliography are quoted for the reader interested in such controversial subjects.

The essential histologic features of all important cutaneous diseases are clearly presented and beautifully depicted in 228 well selected illustrations. The chapter on metabolic diseases is well worth reading, from a clinical or pathological viewpoint. Its faults are too minor to mention. However, continuity in reading would have been simplified by omission of the names of authors of references, and substitution of numbers.

This book will fill an important niche in all medical libraries.

Differential Diagnosis of Chest Diseases. By Jacob J. Singer, M.D. 8°, cloth, 344 pp., with 171 illustrations. Philadelphia: Lea and Febiger, 1949. $7.50.

This book is an excellent short summary of the differential diagnosis of chest diseases by a recognized authority in the field. Under each disease there are sections on etiology, pathology, clinical symptoms, physical signs, roentgen-ray findings, laboratory tests and differential diagnosis. The material is concisely presented, the illustrations are good, and the bibliographies are carefully selected.

Unfortunately, its brevity is such that it will not be very useful as a reference book. A doctor seeking information about any of the chest diseases will not find the answers to many diagnostic questions that he will naturally ask. The twelve short pages on cancer of the lung do not give an adequate picture of this extremely important and confusing disease.

Clinical Interpretation of Laboratory Tests. By Raymond H. Goodale, M.D. 8°, cloth, 605 pp., with 107 illustrations. Philadelphia: F. A. Davis Company, 1949. $6.50.

In a sense physicians have returned to the humoral pathology of Hippocrates. No patient's record is complete until a number of tests on the various body fluids have been done. A blood Wassermann test and blood and urine examinations are general routine in every hospital examination. Other diseases demand certain specific studies.

Here is a book that gives a concise and brief clinical interpretation of laboratory tests. Numerous modern, rapid

advances in all branches of clinical pathology have created a demand for such a book. It is desirable for the physician to know what tests are indicated and what to expect from these tests. On the other hand there is no need to do all kinds of unnecessary procedures on patients whose ailments do not indicate them. This book is up to date and covers all practical tests. It not only considers the routine tests of hematology, blood chemistry, serology and so forth but also includes tests for vitamin deficiency and the Rh factor — it even includes the effects of atomic radiation. Each test is reported briefly and in some cases much too briefly.

This book should be a valuable addition to the library of every practicing physician.

Roentgen-Ray Examination of the Digestive Tract. By Ross Golden, M.D. 8°, cloth, 356 pp., with 117 illustrations. New York: Thomas Nelson and Sons, 1949. $5.00

This monograph, a reprint of the corresponding chapters in the last issue of *Nelson's Loose Leaf Diagnostic Roentgenology*, edited by the author, discusses the roentgen-ray examination of the digestive tract and of the gall bladder. The methods of examination in the various parts of the gastrointestinal tract are described. Disturbances of function in addition to morphologic abnormalities are stressed throughout the volume. The literature on the subject, both old and recent, is used critically. The main value of the book, however, is the fact that it is not a simple extract of the world literatures but represents an account of the personal experiences, observations and conclusions of a master on the subject. For this reason it is interesting reading for the beginner as well as for the experienced examiner.

It probably represents the best book on the subject in the English language, and obviously belongs in the library of each roentgenologist and gastroenterologist.

The volume contains numerous illustrations. It is hoped that in a new edition their number can be still further increased and that the reproductions can be improved.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Urological Aspects of Spinal Cord Injuries. By George C. Prather, M.D., Department of Genitourinary Surgery, Harvard Medical School, Boston. 8°, cloth, 146 pp., with 38 illustrations. Springfield, Illinois: Charles C Thomas, 1949. $3.75. (American Lecture Series No. 30.)

This monograph reviews the pertinent literature on the subject. There is a bibliography of one hundred and sixty-six titles. The small volume should be in all medical libraries and in all collections on urology and neurology.

Operative Technic in Specialty Surgery. Edited by Warren H. Cole, M.D., professor and head of the Department of Surgery, University of Illinois College of Medicine, and director of surgical service, Illinois Research and Educational Hospitals, Chicago. With an introduction by Allen O. Whipple, M.D. 8°, cloth, 725 pp., with 392 illustrations. New York: Appleton–Century–Crofts, Incorporated, 1949. $14.00.

This is a companion volume to the volume on general surgery, previously published in 1949 and already noted in the *Journal*. Twenty-one contributors, specialists in their particular fields, are responsible for lengthy articles on plastic surgery; the thoracic wall, pleural cavity, lungs and diaphragmatic hernia; the heart and mediastinum; fractures; hematogenous osteomyelitis; deformities and neoplasms of bone; surgical approaches to the joints; the orthopedic surgical treatment of spastic paralysis and anterior poliomyelitis; the scalp, cranium, brain and spinal cord; the intracranial and peripheral nerves; the autonomic nervous system (by Dr. Reginald H. Smithwick, of Boston); gynecologic surgery (by Drs. Joe V. Meigs and Langdon Parsons, of Boston); and the male genitourinary system. The work is especially strong in orthopedic surgery and surgery of the nervous system. The book is well published in every way and is an excellent companion to the previous volume on general surgery. There is a good index. The set of two volumes should be in all medical libraries and available to all surgeons.

A Textbook of Physiology: Originally by William H. Howell, M.D. Edited by John F. Fulton, M.D., Sterling Professor of Physiology, Yale University School of Medicine. Sixteenth edition. 8°, cloth, 1258 pp., with 556 illustrations. Philadelphia: W. B. Saunders Company, 1949. $10.00.

This new edition of a standard textbook, first published in 1907 and long known as Howell's textbook, is the joint work of twenty-nine authorities. The text has been thoroughly revised and brought up to date. The chapters on the endocrines have been extensively revised by Dr. Jane Russell, and the section on the electrocardiograms has been completely rewritten. New material includes chapters on the gastrointestinal tract, on muscle, on the cerebrospinal system and on the physiology of micturition. The printing is well done with a new type on light paper, and there is a comprehensive index. The book is recommended for all medical libraries and to all physiologists.

Acute Laryngotracheobronchitis. By A. Harry Neffson, M.D. 8°, cloth, 197 pp., with 17 illustrations. New York: Grune and Stratton, 1949. $5.00.

In this small monograph the author has covered all aspects of the disease under consideration. Seventy-four pages are devoted to treatment. There are special chapters on tension pneumothorax and mediastinal emphysema after tracheotomy, and on obstructive laryngitis associated with the exanthemas. There are indexes of authors and subjects and a bibliography. The publishing is well done.

Almost overnight, small monographs have come into being. They are essentially library books and should be found in all medical libraries, where they may be consulted by all physicians.

Advances in Pediatrics. Volume IV. 8°, cloth, 316 pp. New York: Interscience Publishers, Incorporated, 1949. $6.50.

This fourth volume in an important series contains seven monographs on various aspects of pediatrics by four foreign and six American authorities. The topics discussed comprise diet in diabetes, the treatment of congenital syphilis with penicillin, erythema nodosum, the reticuloendothelioses, combined immunizations, subdural hematoma and cystinosis. A bibliography is appended to each paper, and there are indexes of authors and subjects. Likewise, there is a cumulative index for the series of four volumes. The publishing is excellent. The set should be in all medical libraries and available to all persons interested in the diseases of children. The *Advances* are somewhat akin to the well known German *Ergebnissen*, although not quite so extensive.

Unipolar Lead Electrocardiography: Including standard leads, augmented unipolar extremity leads and multiple unipolar precordial leads, and a section on cardiac arrhythmias. By Emanuel Goldberger, M.D., adjunct physician, Montefiore Hospital, New York City, cardiographer and associate physician, Lincoln Hospital, New York City, consulting cardiologist, St. Joseph's Hospital, Yonkers, New York, and lecturer in medicine, Columbia University College of Physicians and Surgeons. Second edition. 8°, cloth, 392 pp., with 221 illustrations. Philadelphia: Lea and Febiger, 1949. $7.50.

In this new edition the text has been thoroughly revised, and large portions rewritten and simplified. A comprehensive chart, showing the six unipolar precordial leads and the three augmented unipolar extremity leads of normal persons and of all the common abnormalities, and an appendix on some electrocardiographic observations have been added to the text. Likewise, there have been included fifty new electrocardiograms and new chapters on the electrocardiograph, on the measurement of all waves and intervals of the

electrocardiogram and their normal values, and on normal and abnormal cardiac rhythms. The author has incorporated the results of his latest studies on unipolar leads and the recent reports of other investigators, including the autopsy correlation studies of Dr. G. B. Myers and his associates. A bibliography of 437 titles concludes the text. The publishing is excellent, and the book should be available to all interested physicians.

Modern Practice in Ophthalmology, 1949. Edited by H. B. Stallard, M.B.E., M.A., M.D., F.R.C.S., surgeon, Moorfields, Westminster and Central Eye Hospital, London, and eye surgeon, St. Bartholomew's Hospital, London. 8°, cloth, 525 pp., with 231 illustrations and 30 color plates. New York: Paul B. Hoeber, Incorporated, 1949. $12.50. (*Butterworth's Medical Publications, Modern Practice Series.*)

This new book, which is the joint work of twenty-one British authorities, has been written for the general practitioner and presents an outline of present-day ophthalmology. The whole field has been covered, including anatomy and physiology, surgery and tropical ophthalmology. There is a good index. The publishing is well done, and the color work is good. The text was printed in Great Britain.

Functional Localization in Relation to Frontal Lobotomy. By John F. Fulton, O.B.E., M.D., D.Sc., LL.D. (Birm.). 8°, cloth, 140 pp., with 53 illustrations. New York: Oxford University Press, 1949. $3.00. (Being the William Withering Lectures delivered at the Birmingham Medical School, 1948.)

In these four lectures Dr. Fulton reviews functional localization as evidenced by experimental neurology during the past fifteen years. The lectures discuss, in order, the frontal lobes — the precentral motor cortex; the frontal areas and the orbital surface — subhuman primates; the frontal areas and orbital surface — man; and the cerebellum reconsidered. Each lecture is documented with a long list of references. The small book should be in all neurology collections.

Clinical Audiology. By Maurice Saltzman, M.D., assistant professor of otorhinology, Temple University School of Medicine, and associate otolaryngologist, Mount Sinai Hospital, Philadelphia. With an introduction by George M. Coates, M.D., chief editor, *Archives of Otolaryngology.* With a foreword by Matthew S. Ersner, M.D., professor and head of the Department of Otorhinology and Rhinoplasty, Temple University School of Medicine. 8°, cloth, 195 pp., with 82 illustrations. New York: Grune and Stratton, 1949. $5.00.

This book in a new field embodies the work carried out at the hearing clinic of the School of Medicine of Temple University. The fields of hearing and deafness are covered in a concise manner. The text is divided into five parts, in which are discussed sound and noise, hearing, deafness, hearing tests and hearing aids. The monograph should be in all medical libraries and in the collections of otologists.

Roentgen Diagnosis of Diseases of the Skull. By Max Ritvo, M.D., assistant professor of radiology, Harvard Medical School, instructor in radiology, Tufts College Medical School, director, Department of Radiology, Boston City Hospital, and associate in radiology, Beth Israel Hospital. With a foreword by George W. Holmes, M.D. 4°, cloth, 409 pp., with 466 illustrations. New York: Paul B. Hoeber, Incorporated, 1949. $15.00. (*Annals of Roentgenology,* Volume XIX.)

This new volume in an excellent series of atlases is a worthy companion to its predecessors. The material is almost entirely from the files of the Boston City Hospital and includes the rare as well as the common conditions met with in the examination of the skull. Among the rarer cases may be mentioned sinus pericranii, tuberous sclerosis, symmetrical cerebral calcification of the basal ganglions, erythroblastosis fetalis and intracranial lipoma. Short clinical discussions of many of the conditions are included for ready reference purposes. Pneumoencephalography is not discussed. The text is divided into nine parts: roentgenologic examination of the skull; congenital, hereditary and developmental anomalies; traumatic and postoperative changes; infections; nutritional, endocrine, and metabolic disturbances; roentgenologic study of the fetal skull during pregnancy; intracranial calcifications and accumulations of iodized oil, foreign bodies and intraocular calcifications; neoplasms; and cerebral angiography. The section on neoplasms is very extensive, comprising nearly a third of the text. Lists of selected references are appended to the various chapters, and there is a good index. The publishing, including the plate work, is excellent. The atlas is recommended for all medical librari s and should prove valuable to radiologists and brain surgeons.

Everyday Miracle: Through intimate and sympathetic observation of animals, a brilliant scientist illuminates the miracle of all life. By Gustav Ekstein, M.D. 9°, cloth, 235 pp. New York: Harper and Brothers, 1948. $2.75.

The author, in this interesting book, has selected twenty-four themes in the life of man, including old age, hunger, vision, life, smell and sleep, and paralleled them with incidents in the lives of nonhuman creatures. The text is written in a simple manner. The type and printing are excellent. The book is well adapted for the light-reading section of medical libraries and should be in all public libraries.

Hearing Tests and Hearing Instruments. By Leland A. Watson and Thomas Tolan, M.D. 8°, cloth, 597 pp., with 239 illustrations. Baltimore: Williams and Wilkins Company, 1949. $7.00.

This book constitutes a comprehensive work on audiometry and discusses hearing tests in all their aspects. There is a special chapter on hearing aids and the first part deals with the fundamentals of hearing and testing. There is a bibliography of forty-eight pages and also a coded reference index of subjects. The text is concluded with a glossary of terms used in audiology, a list of the 239 illustrations and an index. The publishing is excellent, and the book should be in all medical libraries and available to all persons interested in the subject.

Arterial Hypertension: Its diagnosis and treatment. By Irvine H. Page, M.D., and Arthur C. Corcoran, M.D., Research Division of the Cleveland Clinic Foundation, Cleveland. Second edition. 8°, cloth, 400 pp., with 19 illustrations. Chicago: Year Book Publishers, Incorporated, 1949. $5.00.

This practical book was first published in 1945 and reprinted in 1946. The manual is intended for the practicing physician and does not claim to be an exhaustive treatise. It is composed of recommendations, prescriptions and technics of diagnosis. It forms one of the *General Practice Manuals* and the publishing is excellent. The use of a nonfilled paper would be desirable in future editions.

Malaria: The biography of a killer. By Leon J. Warshaw, M.D. 8°, cloth, 348 pp. New York: Rinehart and Company, Incorporated, 1949. $3.75.

Dr. Warshaw has written a popular history of malaria, "the world's greatest killer." At least 300,000,000 persons a year suffer from malaria and not less than 3,000,000 die from the disease. In India alone a third of the cases and a third of the deaths occur. The great impact of the disease falls upon tropical and subtropical countries situated between the latitudes of 45° North and 40° South, but the remainder of the world is not immune. The disease is responsible for tremendous economic loss. Alexander the Great's conquest of the world was halted by an attack of malaria, and many other great persons were incapacitated by its debilitating effects. From ancient times to the present day, the author relates the story of the disease in all its aspects. The book should be in all medical and public libraries.

A Manual of Physical Therapy. By Richard Kovács, M.D., professor of physical medicine, New York Polyclinic Medical School and Hospital, attending physical therapist, Manhattan State, Harlem Valley State and Columbus hospitals, visiting physical therapist, New York City Department of

Correction Hospitals, consulting physical therapist, Mary Immaculate Hospital, Jamaica, New York, St. Charles Hospital, Jefferson, Long Island, Alexian Brothers Hospital, Elizabeth, New Jersey, area consultant, Veterans Administration, and consultant, physical medicine, Surgeon General, Department of the Army. Fourth edition. 12°, cloth, 328 pp., with 124 illustrations. Philadelphia: Lea and Febiger, 1949. $3.75.

This popular manual has been revised and brought up to date, and a chapter on medical rehabilitation has been added. Its soundness is evidenced by the fact that the previous edition had to be reprinted four times during the past four years. This elementary exposition of physical therapy should prove valuable to all persons interested in the subject.

Clinical Diagnosis by Laboratory Examinations. By John A. Kolmer, M.S., M.D., Dr.P.H., Sc.D., LL.D., L.H.D., professor of medicine in the School of Medicine and the School of Dentistry of Temple University, and director of the Research Institute of Cutaneous Medicine. Second edition. 8°, cloth, 1212 pp., with 93 illustrations and 139 tables. New York: Appleton-Century-Crofts, Incorporated, 1949. $12.00.

The authors have thoroughly revised this standard work to bring it up to date since the publication of the first edition in 1943. Much new material, too extensive to be enumerated, has been incorporated throughout the text. The work is divided into three major parts: the clinical interpretation of laboratory examinations; the practical applications of laboratory examinations in clinical diagnosis; and technic of laboratory examinations. There are a hundred and thirty-nine diagnostic summary tables. There is a valuable, comprehensive index, numbering one hundred and eight pages. Color plates are tipped in, and the publishing is excellent. The book should be in all reference collections on the subject.

The 1949 Year Book of Radiology (June 1948–June 1949). Radiologic Diagnosis. Edited by Fred J. Hodges, M.D., professor and chairman, Department of Roentgenology, University of Michigan Medical School; and John F. Holt, M.D., associate professor, Department of Roentgenology, University of Michigan Medical School. *Radiation Therapy.* Edited by Isadore Lampe, M.D., associate professor, Department of Roentgenology, University of Michigan Medical School. 8°, cloth, 453 pp., with 393 illustrations. Chicago: Year Book Publishers, Incorporated, 1949. $6.50.

This yearbook provides abstracts of the worthwhile articles appearing in scattered sources during the year ending June, 1949. It is notable for the large number of excellent illustrations. There are indexes of subjects and authors, and the publishing is well done. The volume should be in all reference collections on radiology.

The Clinical Examination of the Nervous System. By G. H. Monrad-Krohn, M.D., professor of medicine in the Royal Frederick University, Oslo, physician-in-chief to the University Clinic for Nervous Diseases, Oslo, and consulting physician to the epileptic colony of the Norwegian State. Ninth edition. 12°, cloth, 459 pp., with 131 illustrations. New York: Paul B. Hoeber, Incorporated, 1949. $5.00.

The soundness of this manual is attested by its long publication record. First published in 1921, it has now gone through nine editions and sixteen printings and has been translated into French and Spanish. Material on electroencephalography has been added. The printing was done in Great Britain, and the publishing is excellent.

A Textbook of Surgery. By American authors. Edited by Frederick Christopher, M.D., professor of surgery, Northwestern University Medical School, and chief surgeon, Evanston (Illinois) Hospital. Fifth edition. 4°, cloth, 1550 pp., with 1465 illustrations. Philadelphia: W. B. Saunders Company, 1949. $13.00.

This standard textbook, first published in 1936, is the work of a hundred and ninety-eight contributors, all specialists in their particular fields. The text has been carefully brought up to date, and a great many entirely new sections, too many to enumerate, have been included. Each section is documented with a list of selected references, and the text is concluded with a comprehensive index. The type and printing are excellent, and the use of a lightweight paper reduces the weight of the volume. The book should be in all medical libraries and available to all surgeons.

A Short Practice of Surgery. By Hamilton Bailey, F.R.C.S. (Eng.), F.A.C.S., F.I.C.S., F.R.S.E., surgeon, Royal Northern Hospital, London, senior surgeon, St. Vincent's Clinic and the Italian Hospital, consulting general surgeon, Metropolitan Ear, Nose, and Throat Hospital, and consulting surgeon, Potter's Bar Hospital, Essex County Council and Clacton Hospital; and R. J. McNeill Love, M.S. (Lond.), F.R.C.S. (Eng.), F.A.C.S., F.I.C.S., surgeon, Royal Northern, Mildmay Mission and Metropolitan hospitals, consulting surgeon, City of London Maternity Hospital, consulting surgeon to the London County Council and Potter's Bar Hospital, associate for general surgery, West End Hospital for Nervous Diseases, and member of council and court of examiners, Erasmus Wilson Demonstrator and Hunterian Professor, Royal College of Surgeons. Eighth edition. 8°, cloth, 1050 pp., with 1198 illustrations. Baltimore: Williams and Wilkins Company, 1949. $10.00.

First published in 1932, this popular British textbook on surgery has gone through fourteen printings and eight editions, and a Chinese translation is in preparation. Its printing record during the war years attests its soundness. The printing was done in Great Britain, and the publishing is excellent.

Surgical and Maxillofacial Prosthesis. By Oscar E. Beder. 4°, cloth, 51 pp. Columbia University, New York: King's Crown Press, 1949. $3.00.

This monograph discusses the apparatus and technics used in maxillofacial prosthesis. It is illustrated with thirty-one drawings. It constitutes one of the low-priced publications of the Columbia University Press and should prove of value to dentists and surgeons interested in the mouth and face.

Diseases of the Nervous System: Described for practitioners and students. By F. M. R. Walshe, M.D., D.Sc., F.R.S., fellow of the Royal College of Physicians of London, fellow of University College, London, physician in charge of the Neurological Department, University College Hospital, and physician to the National Hospital for Nervous Diseases, Queen Square. Sixth edition. 8°, cloth, 359 pp., with 60 illustrations. Baltimore: Williams and Wilkins Company, 1949. $5.00.

In this new edition of a standard textbook the chapter on neurosyphilis has been rewritten, and the material on penicillin, acute poliomyelitis and intracranial abscess has been amplified and the other material brought up to date. The first edition was published in 1940, and translations have been made into French and Spanish. The text was printed in Great Britain, and the publishing is excellent.

Medical Meeting. By Mildred Walker. 8°, cloth, 280 pp. New York: Harcourt, Brace and Company, 1949. $3.00.

In her eighth novel and her second of a medical character, Mildred Walker, an outstanding writer, tells the story of a medical meeting, held in Chicago, at which a new drug was announced. The interlocking relationships of a number of married medical couples are portrayed. The story is well written, and the plot is smooth in its movement.

Bibliographia Medica Helvetica. Volume 5, 1947. 8°, paper, 474 pp. Basal, Switzerland: Benno Schwabe and Company, 1949. Broschiert Fr. 15.

This current bibliography of books and articles published in Switzerland during 1947 is sponsored by the Swiss Academy of Medical Sciences. The material is arranged by subjects according to a decimal classification. The complete series should be in the reference collections of large medical libraries.

NOTICES

ANNOUNCEMENT

Dr. Lincoln Lebeaux announces the removal of his office to 6 High Street, Worcester, for the practice of neurology and psychiatry.

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

The following meetings of the Boston City Hospital House Officers Association will be held this month:

Dr. Garfield Duncan, chief of medicine, Pennsylvania Hospital, will present a paper entitled "Nutrition and Chronic Disease" in the Dowling Amphitheater of the Boston City Hospital on Thursday, April 20, at 7 p.m.

Dr. Arthur J. Merrill, associate professor of medicine, Emory University, will present a paper on the subject "Mechanism of Sodium Retention in Heart Failure" in the Dowling Amphitheater on Tuesday, April 25, at 7 p.m. Drs. E. M. Landis, Samuel H. Proger and L. B. Ellis will lead the discussion.

Dr. Samuel Soskin, dean of the Postgraduate School, Michael Reese Hospital, Chicago, will present a paper on the subject "The Theory and Practice of the Treatment of Diabetes" in the Dowling Amphitheater on Thursday, April 27, at 7 p.m. Drs. Alexander Marble and Samuel Beaser will lead the discussion.

All interested persons are invited to attend.

AMERICAN ACADEMY OF DENTAL MEDICINE

The annual meeting of the American Academy of Dental Medicine will be held at the Copley Plaza Hotel, Boston, on Saturday and Sunday, June 24 and 25.

PROGRAM

Saturday, June 24

10:00 a.m. Business Meeting.
12:30 p.m. Luncheon: Presentation of Honorary Membership to Dr. Philip E. Adams, president of the American Dental Association.
2:00 p.m. Enzymology and Biochemistry of the Mouth. Dr. Irving W. Sizer, associate professor of physiochemistry, Massachusetts Institute of Technology.
2:45 p.m. Electromicroscopy. Dr. Cecil E. Hall, associate professor of biophysics, Massachusetts Institute of Technology.
3:30 p.m. Use of Isotopes in Biological Research. Dr. Arthur K. Solomon, associate professor of physiochemistry, Harvard University.

Sunday, June 25

10:00 a.m. Business Meeting.
12:30 p.m. Luncheon.
2:00 p.m. Symposium on Oral Cancer. Dr. Charles C. Lund, president, Massachusetts Section, American Cancer Society, moderator.
Pathology, Physiology and Biology of Cancer. Dr. Ira T. Nathanson.
Cancer Diagnosis: Differential diagnosis, precancerous and nonmalignant. Dr. David Weisberger.
Prevention and Treatment of Cancer, including Surgery and X-Ray Examination. Dr. Thomas J. Anglem.

Information and registration may be obtained on application to Dr. George F. Clarke, chairman, 10 Post Office Square, Boston, Massachusetts.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held in the Conference Room of the hospital on Thursday, May 4, at 7:15 p.m. Dr. Frieda Por will present a case of acromegaly, with discussion by Dr. Oscar Hirsch. Dr. Por will be chairman.

THE SPRINGFIELD HOSPITAL

The following is the educational program of the Springfield Hospital for the next month:

Monday, May 1. 12:00 m. Ophthalmologic Conference on the subject "Vascular Diseases Affecting the Retina" in the Staff Conference Room. Malcolm Bick, M.D.

Thursday, May 4. 12:00 m. Plastic-Surgery Conference on the subject "Modern Concepts in the Management of Hemangioma of the Skin" in the Staff Conference Room. Joseph Baker, M.D.

Tuesday, May 16. 8:30 p.m. Clinicopathological Conference. Staff Conference Room.

Thursday, May 18. 12:00 m. Neurosurgical Conference on the subject "Neurosurgical Problems in General Practice" in the Staff Conference Room. Joseph Hahn, M.D.

Saturday, May 20. 11:00 a.m. Guest Speaker Conference on the subject "Vaginal Hysterectomy" in the Staff Conference Room. Dr. Oliver N. Eastman, professor of gynecology, University of Vermont School of Medicine.

CIVIL SERVICE EXAMINATION FOR MEDICAL OFFICERS

The United States Civil Service Commission has announced examinations for the positions of medical officer and medical officer (specialist). Positions in the former category are for duty in the Panama Canal Service, Public Health Service, Indian Service, Department of the Army, Veterans Administration, Civil Aeronautics Administration, Railroad Retirement Board and other federal agencies, at salaries ranging from $5400 to $6400 a year. Positions as medical officer (specialist) are for duty in various federal agencies located in Washington, D. C., and vicinity, Public Health Service, Children's Bureau and Indian Service located throughout the United States and in the Panama Canal Service, at salaries ranging from $7600 to $10,000 a year. Application Form 57, Card Form 5001-ABC or Form 14 may be obtained from any first-class or second-class post office, or from the Civil Service Regional Office in regional headquarters cities such as Boston and New York, and may be filed at any time with the United States Civil Service Commission, Washington 25, D. C.

SOCIETY MEETINGS AND CONFERENCES

OCTOBER 3–MAY 19. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 286, issue of August 18.

JANUARY 9–DECEMBER 1. Laboratory Courses at Communicable Disease Center, Atlanta, Georgia. Page 950, issue of December 8.

APRIL 20. Boston City Hospital House Officers' Association. Notice above.

APRIL 22–29. American Association of Industrial Physicians and Surgeons. Page 305, issue of February 23.

APRIL 24. Cutter Lecture. Page 567, issue of April 6.

APRIL 24–28. National Tuberculosis Association. Page 678, issue of October 27.

APRIL 25. Massachusetts Public Health Association. Page 568, issue of April 6.

APRIL 25. Hampden District Medical Society. Page 600, issue of April 13.

APRIL 25. Boston City Hospital House Officers' Association. Notice above.

APRIL 25–28. Philadelphia County Medical Society. Page 386, issue of March 9.

APRIL 26. New England Obstetrical and Gynecological Society, Rhode Island Hospital and Providence Lying-in Hospital, Providence, Rhode Island.

APRIL 26. Middlesex South District Medical Society. Page 600, issue of April 13.

APRIL 27. 94th Infantry Division Lecture. Page 528, issue of March 30.

APRIL 27. Boston City Hospital House Officers' Association. Notice above.

APRIL 29. Eastern Section of American Congress of Physical Medicine. Page 306, issue of February 23.

APRIL 29. Long Island College of Medicine Alumni Day. Page 348, issue of March 2.

MAY 1. The Springfield Hospital. Notice above.

MAY 3. Norfolk District Medical Society Anniversary Dinner.

MAY 3–7. Second European Congress of National Associations of Gastroenterology. Page 428, issue of March 16.

MAY 4. Suffolk District Censors' Meeting. Page 234, issue of February 9.

MAY 4. New England Hospital for Women and Children. Notice above.

MAY 4. The Springfield Hospital. Notice above.

MAY 6. Suffolk District Medical Society. Page 600, issue of April 13.

MAY 8. New England Cardiovascular Society. Annual Meeting.

MAY 10. Massachusetts Society of Examining Physicians. Page 528, issue of March 30.

MAY 10. Massachusetts Chapter of American Academy of General Practice. Page 528, issue of March 30.

MAY 10. Suffolk District Medical Society. Page 600, issue of April 13.

(Notices concluded on page xi)

NOTICES (*Concluded from page 640*)

MAY 11. The Problems of Infertility. Dr. David Weintraub. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

MAY 12 AND 13. Meetings at Texas Medical Center. Page 600, issue of April 13.

MAY 14–19. International and Fourth American Congress of Obstetrics and Gynecology. Page 160, issue of January 26.

MAY 16. The Springfield Hospital. Page 640.

MAY 16–18. Massachusetts Medical Society. Annual Meeting. Hotel Statler, Boston.

MAY 17. Luncheon Meeting. Section on Diseases of the Eye, Ear, Nose and Throat, Massachusetts Medical Society. Hotel Statler, Boston. 12:00 m.

MAY 18. The Springfield Hospital. Page 640.

MAY 20. The Springfield Hospital. Page 640.

MAY 22 AND 23. National Research Council Committee on Human Reproduction. Page 488, issue of March 23.

MAY 24–26. American Association of Genito-Urinary Surgeons. Page 234, issue of February 9.

JUNE 12–14. American Neurological Association. Page 600, issue of April 13.

JUNE 22–25. American College of Chest Physicians. Page 270, issue of February 16.

JUNE 24 AND 25. American Society for the Study of Sterility. Page 38, issue of January 5.

JUNE 24 AND 25. American Academy of Dental Medicine. Page 640.

JUNE 26–30. American Physicians Art Association. Page 428, issue of March 16.

JUNE 26–30. American Medical Association. Annual Session. San Francisco, California.

JULY 17–22. International Congress for Scientific Research. Page xvii, issue of September 1.

AUGUST 21–26. International Society of Hematology. Page 888, issue of December 1.

AUGUST 28–SEPTEMBER 1. American Congress of Physical Medicine. Page 428, issue of March 16.

AUGUST 31–SEPTEMBER 7. World Federation for Mental Health. Page 306, issue of February 23.

SEPTEMBER 3–9. International Heart Congress. Page 160, issue of January 26.

SEPTEMBER 27–29. Mississippi Valley Medical Society. Page 991, issue of December 15.

OCTOBER 12–14. American Association of Blood Banks. Page 428, issue of March 16.

NOVEMBER 1. New England Obstetrical and Gynecological Society. Hotel Somerset, Boston.

DISTRICT MEDICAL SOCIETIES

HAMPDEN

APRIL 25. Annual Meeting.

MIDDLESEX SOUTH

APRIL 26. Annual Meeting.

NORFOLK

MAY 3. Anniversary Dinner.

SUFFOLK

MAY 4. Censors' Meeting.
MAY 6. Spring Dinner.
MAY 10. Annual Meeting.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, APRIL 27

THURSDAY, APRIL 27

*9:00–10:00 a.m. Grand Rounds. House of the Good Samaritan.
*7:00 p.m. Boston City Hospital House Officers' Association. Dowling Amphitheater, Boston City Hospital.

FRIDAY, APRIL 28

*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.
*1:30 p.m. Tumor Clinic. Out-Patient Department, Mount Auburn Hospital, Cambridge.

MONDAY, MAY 1

*11:30 a.m.–12:15 p.m. Chest X-Ray Conference. South End Health Unit, 57 East Concord Street, Boston. Dr. Cleaveland Floyd in charge.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

TUESDAY, MAY 2

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.
*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

WEDNESDAY, MAY 3

*11:00 a.m.–12:00 m. Medical Rounds. Children's Medical Center.
*12:00 m. X-Ray Conference. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.
*12:00 m.–1:00 p.m. Clinicopathological Conference (Children's Medical Center). Amphitheater, Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Combined Clinic of all Medical Center Services. Amphitheater, Children's Hospital.

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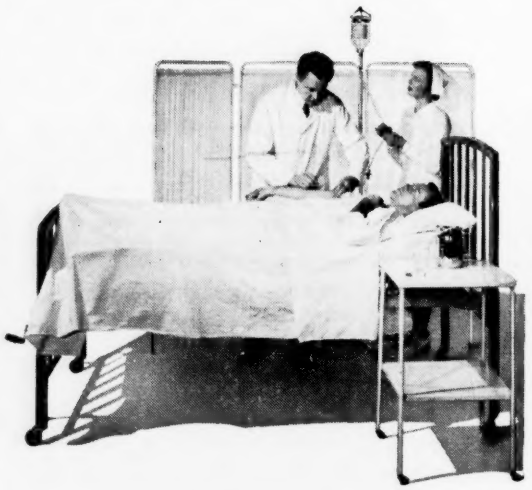

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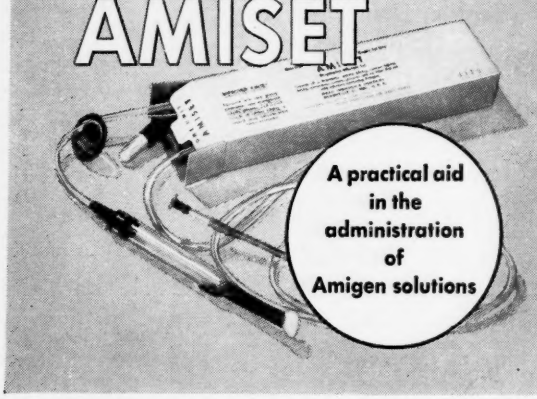

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